510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K160429

B. Purpose for Submission:

Clearance of a new device

C. Manufacturer and Instrument Name:

Shenzhen Mindray Bio-Medical Electronics Co. LTD, BC-5390 Auto Hematology Analyzer

D. Type of Test or Tests Performed:

Complete blood count: WBC ($10^3/\mu L$), RBC ($10^6/\mu L$), HGB (g/dL), HCT (%), MCV (fL), MCH (pg), MCHC (g/dL), RDW-CV (%), RDW-SD, PLT ($10^3/\mu L$), MPV (fL) and leukocyte 5-part differential: Neu#, Lym#, Mon#, Eos#, Bas#, Neu%, Lym%, Mon%, Eos%, Bas%.

E. System Descriptions:

1. Device Description:
   The BC-5390 Auto Hematology Analyzer is a quantitative, automated hematology analyzer and leukocyte differential counter for in vitro diagnostic use in clinical laboratories. It is only to be used by trained medical professionals to identify the normal patient, with all normal system-generated parameters, and to flag or identify patient results that require additional studies. The analyzer provides analysis results for 21 parameters of human blood and three histograms and one scattergram. The BC-5390 Auto Hematology Analyzer system consists of the following components:

   - Sample processing unit (SPU) and Data Managing Unit (DMU)
   - M-53D DILUENT
   - M-5LEO(I) LYSE
   - M-5LEO(II) LYSE
   - M-53LH LYSE
   - Probe Cleanser
   - BC-5D Hematology Control (K160606)
   - SC-CAL PLUS Hematology Calibrator (K955925)

2. Principles of Operation:
   The BC-5390 Auto Hematology Analyzer (hereafter referred to as BC-5390) uses the electrical impedance method to count and measure the size of WBC, RBC, BAS, and

PLT in human whole blood. The WBC, BAS, RBC and PLT parameters are counted in a dedicated channel using the measurement of changes in electrical resistance (i.e., electrical impedance method). These blood cells are suspended in a conductive diluent as the cells pass through an aperture of known dimensions. As each cell passes through the aperture, the change in resistance produces an electrical pulse. The number of generated electrical pulses signal the number of particles (cells) passing the aperture; whereas the amplitude of each pulse is proportional to the volume of each particle. HGB is determined by the colorimetric method, which is measurable at 530-535 nm. The BC-5390 measures the leukocyte differential (Neu, Lym, Mon, Eos) by flow cytometry. As the cells pass through the flow cell they are exposed to a laser beam. The intensity of the light scatter reflects the cell size and intracellular density.

3. Modes of Operation:
   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X___ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X____

4. Specimen Identification:

   Specimen identification is manual entry by keyboard or barcode reader, or automated identification by barcode scanner.

5. Specimen Sampling and Handling:

   The BC-5390 supports three different analysis modes: autoloader whole blood mode, closed whole blood mode, and predilute mode. To analyze a sample in the closed predilute mode, the sample is first manually diluted (20µL of venous or capillary whole blood and 180 µL of diluent) then well-mixed according to the BC-5390 Operator's Manual and presented uncapped to the sample compartment for aspiration. To analyze a sample in the closed whole blood mode, the operator manually presents the sample to the sample compartment. For the autoloader whole blood mode, the operator loads closed tubes into a tube rack (with the respective tube adapter); when analysis begins, the BC-5390 pierces the tube cap and aspirates the sample. All samples processed in each mode should be well-mixed and processed according to the BC-5390 Operator's Manual.

6. Calibration:

   Calibration and verification of calibration with the use of the SC-CAL PLUS calibrator is performed by automated or manual method according to the instructions for use, laboratory procedures, and local or national regulations.

7. Quality Control:

   BC-5D Hematology Control (low, normal and high); K160606

8. Software:

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

   Yes___X____ or No_____

F. Regulatory Information:

1. Regulation section:

   21 CFR § 864.5220, Automated differential cell counter

2. Classification:

   Class II

3. Product code:

   GKZ – Counter, Differential Cell

4. Panel:

   Hematology (81)

G. Intended Use:

1. Indication(s) for Use:
   The BC-5390 Auto Hematology Analyzer is a quantitative, automated hematology analyzer for in vitro diagnostic use in clinical laboratories. The BC-5390 Auto Hematology Analyzer provides complete blood count (WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW-CV, RDW-SD, PLT, MPV) and leukocyte 5-Part differential (Neu#, Lym#, Mon#, Eos#, Bas#, Neu%, Lym%, Mon%, Eos%, Bas%) for whole blood specimens collected in a salt of EDTA [dipotassium (K_2) or tripotassium (K_3)] obtained from venous or capillary blood collection. The purpose of the BC-5390 Auto Hematology Analyzer is to identify the normal human patient, with normal system-generated parameters, from patients whose results require additional studies.

2. Special Conditions for Use Statement(s):
   For prescription use only.

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:
   Sysmex XE-2100 Automated Hematology Analyzer (K992875)

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Intended Use	The BC-5390 Auto Hematology Analyzer is a quantitative, automated hematology Analyzer for in vitro diagnostic use in clinical laboratories. The BC-5390 Auto Hematology Analyzer provides complete blood count (WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW-CV, RDW-SD, PLT, MPV) and leukocyte 5-Part differential (Neu#, Lym#, Mon#, Eos#, Bas#, Neu%, Lym%, Mon%, Eos%, Bas%) for whole blood specimens, collected in a salt of EDTA [dipotassium (K_2) or tripotassium (K_3)] obtained from venous or capillary blood collection. The purpose of the BC-5390 Auto Hematology Analyzer is to identify the normal human patient, with normal system-generated parameters, from patients whose results require additional studies.	The Sysmex XE-2100 is a multi-parameter hematology analyzer intended to classify the following formed elements in EDTA anti-coagulated blood. WBC, Neut%, Neut#, Lymph%, Lymph#, Mon%, Mono#, Eo%, Eo#, Baso%, Baso#, NRBC%, NRBC#, RBC, HGB, HCT, MCV, MCH, MCHC, RDW-CV, RDW-SD, RET%, RET#, IRF, PLT, MPV
Sample Type	Whole Blood	Same
Sample Processing	Automatic sampling, diluting and mixing device	Same
Sample Identification	Manual or automatic barcode scanning of sample tube Manual keyboard entry	Same
Software Risk Level	Moderate	Same

Differences		
Item	Device	Predicate
Test Principle (Lym%, Mon%, Eos%, Neu%)	Flow cytometry method with a semiconductor laser. A 2-dimensional scattergram is obtained from the signal collected by the low-angle scattered light and the high-angle scattered light in which x-axis represents the intracellular density and y-axis the	Flow cytometry method with a semiconductor laser. The lateral-scattered light and lateral fluorescent light are detected in DIFF, and 2-dimensional scattergram are generated.

Differences		
Item	Device	Predicate
	blood cell size.	
Test Principle (WBC/Bas%)	WBC: Electrical impedance and flow cytometry Bas%: Electrical impedance	Flow cytometry method with a semiconductor laser
Test Principle	RBC/PLT: Electrical impedance HGB: Colorimetric method	RBC/PLT: Sheath flow DC detection method HGB: SLS-Hgb method
Throughput	Closed Whole Blood Mode: maximum of 51 samples/hour Autoloader Whole Blood Mode: maximum of 60 samples/hour Closed Predilute Mode: maximum of 53 samples/hour	CBC, CBC+DIFF: Approx. 150 samples/hour Mode with NRBC, RET: Approx. 113-150 samples/hour
Sample Assignment Mechanism	Sample assignment syringe	Sample rotary valve (SRV)
Drive Source Unit	Pump	Pneumatic unit

I. Special Control/Guidance Document Referenced (if applicable):

CLSI H26-A2, Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Proposed Standard – Second Edition

CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

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

CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition

CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

CLSI EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition

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

CLSI EP25-A, Evaluation of Stability of *In Vitro* Diagnostic Reagents; Approved Guideline

CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

J. Performance Characteristics*:*

1. Analytical Performance:

a. Method Comparison

Method comparison studies were performed at three clinical sites (one site in U.S. and two sites in China) to assess the performance of the BC-5390 analyzer compared to the Sysmex XE-2100 using a total of 1,531 native venous whole blood samples collected in K_2EDTA. The study population consisted of 57.1% males and 42.6% females including pediatric (i.e. neonates, infants, children, and adolescents) and adult subjects up to 100 years of age. The gender for 0.3% of the study population (5 samples) was reported as unknown. In addition to healthy individuals, subjects with the following clinical conditions were included in the studies: acute inflammation/bacterial infection, chronic inflammation, parasitic infection/allergic reaction, viral infections, lymphoma, acute lymphoblastic leukemia (ALL), acute myeloblastic leukemia (AML), chronic lymphoblastic leukemia (CLL), chronic myeloblastic leukemia (CML), plasma cell leukemia, other unidentified leukemias, severe anemia, myeloproliferative disorders, aplastic anemia, HIV (human immunodeficiency virus), macrocytic anemia, microcytic/hypochromic anemias, and normocytic/normochromic anemias. Each whole blood sample was analyzed in duplicate on the BC-5390 and Sysmex XE-2100 analyzers.

Deming regression and weighted Deming regression were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals and correlation coefficient) according to CLSI EP09-A3. Weighted Deming regression was used for the WBC, RBC, HGB, and PLT parameters. Deming regression was used for the following parameters: HCT, MCV, MCH, MCHC, RDW-CV, RDW-SD, Neu#, Lym#, Mon#, Eos#, Bas#, Neu%, Lym%, Mon%, Eos%, and Bas%. Bias between the BC-5390 and Sysmex XE-2100 was calculated from the regression line at multiple clinical evaluation points for each parameter. Confidence limits of bias estimates were calculated based on standard errors of bias and 95% confidence. In addition, the mean difference and percent differences for each parameter at the defined clinical evaluation points were calculated. The Bland-Altman (difference) plots and 95% limits of agreement (LOA), and the hypothesis test to the slope and intercept were analyzed by statistical software. The estimated average bias for each parameter was provided for each clinical site and for all sites combined.

Correlation and Estimated Bias of BC-5390 Compared to Sysmex XE-2100 – Combined Sites (excluding flagged parameters)

Parameter	(r)	Slope	95% CI		Intercept (95% CI)	95% CI		Mean	
			Lower Limit	Upper Limit		Lower Limit	Upper Limit	XE-2100	BC-3600
WBC	0.999	1.006	0.990	1.021	-0.075	-0.212	0.062	10.246	10.23

Parameter	(r)	Slope	95% CI		Intercept (95% CI)	95% CI		Mean	
			Lower Limit	Upper Limit		Lower Limit	Upper Limit	XE-2100	BC-3600
Neu#	0.999	1.011	0.997	1.025	-0.292	-0.094	0.036	5.359	5.388
Lym#	0.993	0.975	0.964	0.986	-0.013	-0.034	0.009	2.013	1.95
Mon#	0.966	0.930	0.891	0.969	0.027	0.011	0.043	0.466	0.461
Eos#	0.995	0.994	0.960	1.028	9.386E-04	-0.004	0.006	0.186	0.186
Bas#	0.624	0.916	0.227	1.605	0.007	-0.006	0.020	0.021	0.025
Neu%	0.995	0.984	0.976	0.992	1.487	0.960	2.013	61.97	62.48
Lym%	0.995	0.990	0.981	0.998	-0.272	-0.486	0.058	28.06	27.50
Mon%	0.930	0.965	0.930	1.000	0.226	0.038	0.413	5.855	5.877
Eos%	0.994	0.988	0.969	1.006	0.027	-0.014	0.068	2.497	2.493
Bas%	0.415	0.431	0.2936	0.568	0.215	0.182	0.247	0.272	0.332
RBC	0.997	1.004	0.999	1.008	-0.002	-0.018	0.014	4.238	4.255
HGB	0.998	1.010	1.005	1.014	-0.055	-0.102	0.008	12.2	12.258
HCT	0.995	1.013	1.006	1.019	-0.567	-0.799	0.335	37.303	37.209
MCV	0.993	1.036	1.029	1.043	-3.763	-4.368	3.158	88.776	88.233
MCH	0.977	1.020	1.008	1.032	-0.545	-0.885	0.205	29.531	29.578
MCHC	0.825	1.184	1.130	1.238	-5.834	-7.657	4.010	33.228	33.509
RDW-CV	0.978	1.024	1.004	1.044	-0.190	-0.481	0.102	15.005	15.17
RDW-SD	0.988	0.988	0.976	0.999	-0.089	-0.634	0.455	48.133	47.458
PLT	0.996	1.019	1.012	1.026	-1.157	-2.215	0.100	288.512	292.552
MPV	0.951	1.057	1.037	1.078	-0.774	-0.996	0.552	10.661	10.496

After analysis, three blood smears were prepared from each sample according to the respective laboratory standard operating procedures. Utilizing manual light microscopy, two readers each performed a 200-cell (leukocyte) differential (including morphology evaluation) for each sample. The overall morphology and distributional flagging efficiency (agreement), false positive (FP) and false negative (FN) rates, as well as clinical sensitivity and specificity were determined using a total of 1,514 whole blood samples.

WBC Distribution Flagging

Combined Sites	Manual					95% CI (Clopper-Pearson)	95% CI (Wilson Score)
BC-5390	P	N	Total	Efficiency	79.1%	77.0% – 81.2%	77.0% – 81.1%
P	850	80	930	FP%	18.7%	15.1% – 22.7%	15.3% – 22.7%
N	236	348	584	FN%	21.7%	19.3% – 24.3%	19.4% – 24.3%
Total	1086	428	1514	Sensitivity	78.3%	75.7% – 80.7%	75.7% – 80.6%
				Specificity	81.3%	77.3% – 84.9%	77.3% – 84.7%

WBC Morphology Flagging

Combined Sites	Manual					95% CI (Clopper-Pearson)	95% CI (Wilson Score)
BC-5390	P	N	Total	Efficiency	88.1%	86.4% – 89.7%	86.4% – 89.6%
P	86	167	253	FP%	11.8%	10.2% – 13.6%	10.2% – 13.6%
N	13	1248	1261	FN%	13.1%	7.2% – 21.4%	7.8% – 21.2%
Total	99	1415	1514	Sensitivity	86.9%	78.6% – 92.8%	78.8% – 92.2%
				Specificity	88.2%	86.4% – 89.8%	86.4% – 89.8%

Overall WBC Flagging						95% CI (Clopper-Pearson)	95% CI (Wilson Score)
Combined Sites	**Manual**			Efficiency	80.6%	78.5% – 82.5%	78.5% – 82.5%
BC-5390	P	N	Total	FP%	21.7%	19.4% – 24.2%	19.5% – 24.1%
P	283	260	543	FN%	10.7%	7.5% – 14.7%	7.8% – 14.6%
N	34	937	971	Sensitivity	89.3%	85.3% – 92.5%	85.4% – 92.2%
Total	317	1197	1514	Specificity	78.3%	75.8% – 80.6%	75.9% – 80.5%

b. Precision/Reproducibility:

Precision performance of the BC-5390 was evaluated by performing a repeatability study at one clinical laboratory site with three analyzers and three operators and reproducibility studies across three clinical laboratory sites.

The repeatability study was conducted at one external clinical laboratory site using multiple operators and three BC-5390 analyzers over multiple operating days. Residual native whole blood samples collected in K_2EDTA collection tubes were selected within the defined ranges and around medical decision points per CLSI H26-A2. Each sample was analyzed 10 consecutive times in the closed whole blood CBC+DIFF and predilute CBC+DIFF modes.

To obtain measures of reproducibility imprecision (%CV and SD), three levels of commercial quality control (single lot) were analyzed over 20 operating days, two runs per day and two replicates per run across three sites (one analyzer per site). To further demonstrate precision performance %CV and SD of within-run, between-run, between-day, and within-device were calculated per site and for the combined sites as shown below.

Reproducibility for Combined Sites – BC-5D Low Level Control (N=240)

Parameter	Mean	Within-run		Between-run		Within-day		Between-day		Within-device		Between-device		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC	3.44	0.07	1.96	0.03	0.99	0.06	1.70	0.02	0.53	0.08	2.26	0.05	1.42	0.09	2.66
Neu#	1.75	0.04	2.48	0.02	1.33	0.04	2.20	0.02	0.96	0.05	2.97	0.03	1.78	0.06	3.46
Lym#	1.34	0.04	3.12	0.00	0.00	0.03	2.08	0.02	1.35	0.05	3.40	0.01	0.70	0.05	3.47
Mon#	0.19	0.02	8.49	0.00	0.00	0.01	5.61	0.01	3.70	0.02	9.26	0.02	8.99	0.02	12.91
Eos#	0.16	0.01	8.92	0.01	5.22	0.01	8.19	0.00	0.00	0.02	10.34	0.00	1.00	0.02	10.38
Bas#	0.80	0.02	2.76	0.01	0.95	0.02	2.17	0.00	0.00	0.02	2.92	0.01	1.37	0.03	3.22
Neu%	50.92	0.91	1.79	0.00	0.00	0.62	1.22	0.33	0.64	0.97	1.90	0.15	0.29	0.98	1.92
Lym%	38.76	0.93	2.41	0.00	0.00	0.57	1.48	0.45	1.16	1.04	2.67	0.55	1.41	1.17	3.02
Mon%	5.54	0.44	7.90	0.00	0.00	0.28	5.13	0.20	3.52	0.48	8.65	0.42	7.59	0.64	11.50
Eos%	4.77	0.37	7.71	0.24	4.96	0.35	7.37	0.00	0.00	0.44	9.17	0.00	0.00	0.44	9.17
Bas%	23.16	0.41	1.77	0.15	0.66	0.33	1.41	0.00	0.00	0.44	1.89	0.00	0.00	0.44	1.89
RBC	2.49	0.02	1.00	0.01	0.24	0.02	0.75	0.02	0.76	0.03	1.28	0.06	2.22	0.06	2.56
HGB	6.02	0.06	0.93	0.03	0.48	0.05	0.82	0.05	0.78	0.08	1.31	0.03	0.45	0.08	1.38
HCT	18.64	0.19	1.03	0.12	0.64	0.18	0.97	0.19	1.03	0.30	1.58	0.47	2.54	0.56	2.99
MCV	74.75	0.16	0.21	0.36	0.49	0.38	0.51	0.41	0.54	0.57	0.76	0.72	0.96	0.92	1.23
MCH	24.13	0.21	0.87	0.07	0.27	0.16	0.67	0.03	0.11	0.22	0.92	0.44	1.84	0.50	2.06
MCHC	32.28	0.28	0.87	0.12	0.36	0.23	0.71	0.20	0.62	0.37	1.13	0.75	2.34	0.84	2.59
RDW-CV	13.70	0.13	0.93	0.06	0.42	0.11	0.78	0.11	0.80	0.18	1.30	0.07	0.49	0.19	1.39

Parameter	Mean	Within-run		Between-run		Within-day		Between-day		Within-device		Between-device		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
RDW-SD	38.86	0.36	0.93	0.04	0.09	0.26	0.66	0.17	0.44	0.40	1.03	0.31	0.81	0.51	1.31
PLT	53.28	3.24	6.09	0.00	0.00	2.20	4.12	1.96	3.68	3.79	7.12	1.37	2.57	4.03	7.57
MPV	10.01	0.46	4.60	0.07	0.72	0.33	3.33	0.00	0.00	0.47	4.65	0.23	2.28	0.52	5.18

Reproducibility for Combined Sites – BC-5D Normal Level Control (N=240)

Parameter	Mean	Within-run		Between-run		Within-day		Between-day		Within-device		Between-device		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC	7.53	0.12	1.64	0.04	0.52	0.10	1.27	0.08	1.01	0.15	1.99	0.03	0.38	0.15	2.03
Neu#	4.40	0.09	2.07	0.00	0.00	0.06	1.35	0.05	1.13	0.10	2.36	0.03	0.62	0.11	2.44
Lym#	2.17	0.05	2.39	0.03	1.24	0.05	2.10	0.03	1.18	0.06	2.94	0.03	1.31	0.07	3.22
Mon#	0.40	0.02	5.97	0.01	1.90	0.02	4.63	0.02	4.48	0.03	7.70	0.03	7.50	0.04	10.75
Eos#	0.56	0.03	5.24	0.01	2.42	0.02	4.42	0.01	1.58	0.03	5.98	0.00	0.00	0.03	5.98
Bas#	2.02	0.04	1.94	0.01	0.36	0.03	1.42	0.02	0.78	0.04	2.12	0.01	0.30	0.04	2.14
Neu%	58.42	0.60	1.03	0.24	0.42	0.49	0.84	0.00	0.00	0.65	1.11	0.12	0.21	0.66	1.13
Lym%	28.80	0.59	2.04	0.00	0.00	0.41	1.42	0.27	0.93	0.65	2.24	0.51	1.75	0.82	2.85
Mon%	5.32	0.30	5.55	0.10	1.80	0.23	4.32	0.25	4.61	0.40	7.44	0.38	7.12	0.55	10.29
Eos%	7.46	0.38	5.07	0.14	1.93	0.30	4.07	0.00	0.00	0.40	5.42	0.00	0.00	0.40	5.42
Bas%	26.88	0.27	0.99	0.12	0.46	0.22	0.83	0.00	0.00	0.29	1.09	0.00	0.00	0.29	1.09
RBC	4.70	0.05	0.96	0.02	0.50	0.04	0.85	0.05	1.03	0.07	1.50	0.00	0.00	0.07	1.50
HGB	13.41	0.08	0.61	0.08	0.62	0.10	0.76	0.14	1.08	0.19	1.39	0.05	0.34	0.19	1.43
HCT	40.75	0.37	0.90	0.34	0.83	0.43	1.05	0.49	1.21	0.70	1.72	0.37	0.91	0.79	1.95
MCV	86.67	0.17	0.20	0.39	0.45	0.41	0.48	0.31	0.36	0.53	0.61	0.79	0.92	0.95	1.10
MCH	28.51	0.21	0.74	0.00	0.00	0.15	0.53	0.05	0.18	0.22	0.77	0.11	0.39	0.25	0.86
MCHC	32.90	0.23	0.69	0.13	0.39	0.21	0.63	0.11	0.35	0.29	0.87	0.18	0.54	0.34	1.02
RDW-CV	13.39	0.11	0.85	0.00	0.00	0.07	0.52	0.13	1.00	0.18	1.31	0.11	0.80	0.21	1.54
RDW-SD	43.74	0.33	0.74	0.01	0.03	0.23	0.53	0.23	0.52	0.40	0.91	0.56	1.28	0.69	1.57
PLT	262.45	5.63	2.15	2.20	0.84	4.55	1.73	5.38	2.05	8.09	3.08	0.00	0.00	8.09	3.08
MPV	10.59	0.15	1.41	0.00	0.00	0.10	0.91	0.17	1.65	0.23	2.17	0.09	0.83	0.25	2.32

Reproducibility for Combined Sites – BC-5D High Level Control (N=240)

Parameter	Mean	Within-run		Between-run		Within-day		Between-day		Within-device		Between-device		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC	15.98	0.20	1.26	0.08	0.48	0.16	1.02	0.14	0.90	0.26	1.62	0.09	0.57	0.27	1.72
Neu#	10.34	0.15	1.47	0.03	0.32	0.11	1.09	0.07	0.71	0.17	1.67	0.05	0.53	0.18	1.75
Lym#	3.08	0.08	2.51	0.03	1.10	0.06	2.09	0.06	1.86	0.10	3.31	0.00	0.00	0.10	3.31
Mon#	0.92	0.05	5.94	0.00	0.00	0.03	3.78	0.02	2.72	0.06	6.53	0.04	4.54	0.07	4.55
Eos#	1.65	0.06	3.81	0.04	2.27	0.06	3.52	0.01	0.79	0.07	4.51	0.01	0.64	0.07	4.55
Bas#	4.91	0.07	1.38	0.01	0.30	0.05	1.02	0.04	0.83	0.08	1.64	0.03	0.58	0.09	1.74
Neu%	64.69	0.50	0.77	0.20	0.31	0.41	0.63	0.20	0.31	0.57	0.89	0.12	0.19	0.59	0.91
Lym%	19.30	0.44	2.28	0.10	0.53	0.33	1.70	0.22	1.14	0.50	2.61	0.08	0.44	0.51	2.64
Mon%	5.73	0.33	5.84	0.00	0.00	0.21	3.66	0.16	2.86	0.37	6.51	0.25	4.33	0.45	7.82
Eos%	10.28	0.35	3.43	0.22	2.18	0.34	3.26	0.00	0.00	0.42	4.06	0.00	0.00	0.42	4.06
Bas%	30.70	0.17	0.56	0.00	0.00	0.11	0.36	0.08	0.25	0.19	0.61	0.00	0.00	0.19	0.61
RBC	5.31	0.05	0.99	0.02	0.36	0.04	0.78	0.05	0.93	0.07	1.41	0.02	0.28	0.08	1.43
HGB	16.85	0.11	0.66	0.08	0.48	0.11	0.67	0.17	1.02	0.22	1.30	0.10	0.62	0.24	1.44
HCT	50.93	0.47	0.93	0.28	0.54	0.43	0.85	0.64	1.26	0.84	1.66	0.50	0.97	0.98	1.92
MCV	95.86	0.19	0.19	0.40	0.42	0.42	0.44	0.37	0.38	0.57	0.60	0.86	0.89	1.03	1.07
MCH	31.70	0.23	0.73	0.08	0.27	0.18	0.58	0.03	0.11	0.25	0.78	0.22	0.68	0.33	1.04

Parameter	Mean	Within-run		Between-run		Within-day		Between-day		Within-device		Between-device		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
MCHC	33.08	0.23	0.69	0.12	0.37	0.20	0.61	0.12	0.36	0.28	0.86	0.14	0.43	0.32	0.96
RDW-CV	12.78	0.10	0.75	0.06	0.50	0.09	0.73	0.15	1.19	0.19	1.49	0.10	0.75	0.21	1.67
RDW-SD	45.52	0.33	0.72	0.10	0.22	0.25	0.55	0.25	0.55	0.42	0.93	0.54	1.18	0.68	1.50
PLT	508.65	8.36	1.64	4.18	0.82	7.24	1.42	7.09	1.39	11.73	2.31	3.89	0.76	12.36	2.43
MPV	10.44	0.08	0.78	0.01	0.06	0.06	0.55	0.12	1.14	0.14	1.38	0.11	1.04	0.18	1.73

c. Linearity:

The linear ranges for the WBC and PLT parameters were established by testing two different sample sets (for each parameter with a wide overlap) prepared by diluting FDA cleared commercially available linearity materials to span the analytical measuring range (AMR). For each sample set, seven proportional dilutions were prepared (0%, 10%, 20%, 40%, 60%, 80%, and 100%). Three replicates were performed for each theoretical concentration on three different BC-5390 analyzers in the closed mode.

The linear ranges for the RBC, HGB, and HCT parameters were established by testing diluted samples prepared from native whole blood. For each parameter, seven proportional dilutions were prepared (0%, 10%, 20%, 40%, 60%, 80%, and 100%). Three replicates were performed for each dilution on two different BC-5390 analyzers in the closed mode.

Polynomial regression analyses for the first, second and third-order polynomials were performed for each evaluated parameter.

Parameter	Analytical Measurement Range (AMR)
WBC ($x10^3/\mu L$)	0.3–200
RBC ($x10^6/\mu L$)	0.20–8.00
HGB (g/dL)	0.5–25.0
HCT (%)	2.0–75.0
PLT ($x10^3/\mu L$)	5–2000

d. Carryover:

Carryover studies for the WBC, RBC, HGB, HCT, and PLT parameters were conducted using high target value (HTV) and low target value (LTV) contrived native whole blood samples. Testing was conducted to evaluate the carryover of whole blood within-mode, predilute within-mode, and mode-to-mode.

For within-mode carryover, the following combinations were evaluated: whole blood CBC+DIFF to whole blood CBC+DIFF and predilute CBC+DIFF to predilute CBC+DIFF. For mode-to-mode carryover, the following combinations were evaluated: whole blood CBC+DIFF to whole blood CBC mode, whole blood CBC+DIFF to predilute CBC+DIFF mode, whole blood CBC+DIFF to predilute

CBC mode, predilute CBC+DIFF to predilute CBC mode, predilute CBC+DIFF to whole blood CBC+DIFF, and predilute CBC+DIFF to whole blood CBC mode.

For each of the mode-to-mode and within-mode combinations the HTV samples (H1, H2, and H3) were aspirated and analyzed three times consecutively followed by three aspirations of the LTV samples (L1, L2, and L3). Carryover % was determined using the following calculation: % Carryover = 10 (LTV1−LTV3) / (HTV3−LTV3) × 100. The results of the carryover study were within the predefined specifications of ≤ 1.0% for WBC, RBC, HGB, HCT and PLT.

e. Interfering Substances:

Interfering substance studies were performed for the following: bilirubin, hemoglobin, triglycerides, high WBC, and high PLT. Whole blood samples (K_2EDTA) within the defined reference ranges were spiked with each interferent at different concentrations.

There was no significant bilirubin interference up to a concentration 500 mg/L for the following parameters: WBC, Neu#, Lym#, Mon#, Eos#, Bas#, Neu%, Lym%, Mon%, Eos%, Bas%, RBC, HCT, MCV, RDW-CV, RDW-SD, PLT and MPV parameters.

There was no significant hemoglobin interference up to a concentration 1110 mg/dL for the following parameters: WBC, Neu#, Lym#, Mon#, Eos#, Bas#, Neu%, Lym%, Mon%, Eos%, Bas%, RBC, HCT, MCV, RDW-CV, RDW-SD, PLT and MPV parameters. There was no significant hemoglobin interference up to a concentration 751 mg/dL for the HGB parameter; up to a concentration 693 mg/dL for the MCH parameter; and up to a concentration of 677 mg/dL for the MCHC parameter.

There was no significant triglyceride interference up to a concentration of 29.4 mmol/L for the HCT and MCV parameters. There was no significant triglyceride interference up to a concentration of 20 mmol/L for the HGB and MCH parameters and up to a concentration of 25 mmol/L for the MCHC parameter.

There was no significant interference observed for WBC up to a concentration of 183.72 x 10^3/µL for the following parameters: HGB, HCT, MCV, MCH, and MCHC.

There was no significant interference observed for PLT up to a concentration of 1809 x 10^3/µL for the following parameters: HGB, HCT, MCV, MCH, and MCHC.

2. Other Supportive Instrument Performance Data Not Covered Above:

a. Specimen Stability

To evaluate sample stability for the whole blood mode (closed and autoloader) a combination of freshly collected whole blood samples drawn from patients and residual whole blood samples from clinical laboratory sites were analyzed. The

sample size totaled 54 specimens spanning the defined analytical measurement range for the WBC, RBC, HGB, and PLT parameters in addition to clinical evaluation points for other measurands. Aliquots were prepared and stored at the defined condition for each specimen, then analyzed in duplicate at different time points according to the study design. The sample stability for all measurands analyzed in the whole blood mode at room temperature (18–26°C) and refrigerated temperature (2–8°C) was established at 24 hours and 36 hours from the time of collection respectively.

Sample stability for the closed predilute mode was evaluated using a total of 35 residual whole blood samples spanning the defined analytical measurement range for the WBC, RBC, HGB, and PLT parameters in addition to clinical evaluation points for other measurands. Aliquots were prepared and stored at the defined condition for each specimen, then analyzed in duplicate at different time points according to the study design. The sample stability at room temperature for all measurands was established at 25 minutes from the time of sample preparation (dilution).

Acceptance criteria for each parameter was established for defined time intervals at each storage condition as the difference between the recovery of the measurand at defined time points and time point zero (T0). The acceptance criteria were met for each claimed storage condition: 25 minutes for prediluted samples, 24 hours for whole blood samples stored at room temperature (18–26°C) and 36 hours for whole blood samples stored at refrigerated temperature (2–8°C).

b. Sample Matrix Comparison

To demonstrate matrix equivalency of capillary whole blood to venous whole blood, a matrix comparison study was conducted using 57 paired samples collected in K_2EDTA. The samples were selected to cover the analytical measurement range of the WBC, RBC, HGB, and PLT parameters in addition to the medical decision levels of other measurands. Deming and weighted Deming approaches were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals and correlation coefficient) according to CLSI EP09-A3. Confidence limits of bias estimates were calculated based on standard errors of bias and 95% confidence intervals. The results of the Deming and weighted Deming regression analyses and bias between the paired samples on the BC-5390 analyzer met the defined acceptance criteria for all parameters.

c. Mode Comparison

To demonstrate sample equivalency between the whole blood mode and predilute mode, a comparison study was conducted using 124 residual samples collected in K_2EDTA. The samples were selected to cover the analytical measuring range of the WBC, RBC, HGB, and PLT parameters in addition to the medical decision levels of other measurands.

For the comparison of the CBC whole blood mode to the CBC+DIFF whole blood mode, a total of 103 samples were analyzed in duplicate in each mode. Similarly, for the comparison between the CBC predilute and the CBC+DIFF predilute modes, a total of 75 samples were analyzed in duplicate in each mode. The samples were selected to cover the analytical measurement ranges of the WBC, RBC, HGB, and PLT parameters in addition to clinical evaluation points of the other parameters.

Deming and weighted Deming approaches were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals and correlation coefficient) according to CLSI EP09-A3. Results for each comparison and parameter met the defined acceptance criteria.

d. Anticoagulant Comparison

To demonstrate equivalency between samples collected in K_3EDTA versus those collected in K_2EDTA, a comparison study was conducted using 70 paired samples collected in K_2EDTA and K_3EDTA. The samples were selected to cover the normal range and medical decision levels for all measurands. Deming and weighted Deming approaches were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals and correlation coefficient) according to CLSI EP09-A3. Results for each comparison and parameter met the defined acceptance criteria.

e. Limits of Detection, Blank, and Quantitation (LoD, LoB, and LoQ)

Limit of Blank (LoB) was determined using five blank samples containing the predilute solution (diluent). Each blank sample was analyzed 12 times in the whole blood and predilute modes on three BC-5390 analyzers at one clinical laboratory site. To determine the Limit of Detection (LoD) and Limit of Quantitation (LoQ), five low level samples were derived from native whole blood. Each low level sample was analyzed 12 times in the whole blood and predilute modes on three BC-5390 analyzers at one clinical laboratory site.

	Whole Blood Mode			**Predilute Mode**		
Parameter	LoB	LoD	LoQ	LoB	LoD	LoQ
WBC ($x10^3/\mu L$)	0.00	0.03	0.03	0.01	0.06	0.06
PLT ($x10^3/\mu L$)	0.00	3.0	3.0	0.00	2.5	2.5

f. Background Counts

To establish the allowable background count for the BC-5390, diluent was analyzed as a sample in the whole blood and predilute modes, one run per day over multiple operating days at three clinical laboratory sites.

Parameter	Background Specifications
WBC	≤ 0.1 x 10^3/µL
RBC	≤ 0.02 x 10^6/µL
HGB	≤ 0.1 g/dL
PLT	≤ 5 x 10^3/µL

g. Adult Reference Intervals

The adult reference interval for each BC-5390 parameter was established by analyzing whole blood samples collected in K_2EDTA from a total population of 251 healthy individuals (N=121 males, and N=130 females) representative of the United States population (i.e. race demographics). Due to the sample size of each gender (N≥120), confidence intervals for each parameter were calculated using a 90% probability (90% CI).

Parameter	Male (N=121)		Female (N=130)		Overall (N=251)	
	Lower Limit	Upper Limit	Lower Limit	Upper Limit	Lower Limit	Upper Limit
WBC (x10^3/µL)	3.782	12.049	4.374	11.193	3.972	11.726
Neu# (x10^3/µL)	1.744	9.728	2.229	8.363	2.029	8.578
Lym# (x10^3/µL)	1.181	4.268	1.288	3.778	1.214	3.858
Mon# (x10^3/µL)	0.210	0.869	0.211	0.667	0.210	0.787
Eos# (x10^3/µL)	0.031	0.599	0.023	0.487	0.030	0.557
Bas# (x10^3/µL)	0.010	0.100	0.010	0.080	0.010	0.080
Neu%	39.06	78.14	41.94	76.49	41.33	76.90
Lymph%	14.13	50.47	16.14	49.67	15.13	49.84
Mon%	3.61	10.90	3.63	8.87	3.63	9.77
Eos%	0.41	8.82	0.40	8.12	0.40	8.10
Bas%	0.20	1.20	0.20	1.00	0.20	1.10
RBC (x10^6/µL)	4.231	6.219	3.728	5.454	3.907	6.021
HGB (g/dL)	13.01	18.28	10.18	16.27	10.68	17.47
HCT (%)	38.50	54.13	31.93	47.30	33.81	51.47
MCV (fL)	74.28	100.68	74.33	96.87	74.33	97.64
MCH (pg)	24.96	34.54	23.36	32.40	23.90	33.18
MCHC (g/dL)	32.01	36.00	30.80	35.87	31.02	35.90
RDW-CV (%)	12.01	17.39	11.80	18.63	12.00	17.67
RDW-SD	36.74	55.63	37.08	56.00	37.09	55.55
PLT (x10^3/µL)	141.1	456.6	186.4	405.5	147.7	435.4
MPV (fL)	9.30	14.26	9.30	13.59	9.30	13.61

h. Pediatric Reference Interval Verification

A literature reference interval verification study was performed for the pediatric population. A total of 161 samples were collected from apparently healthy pediatric patients ranging from neonate to 21 years of age within each pediatric subcategory (see table below). The results of the WBC, Neu#, Lym#, Eos#, Bas#, RBC, HGB,

HCT, MCV, and PLT parameters were compared to literature pediatric reference intervals.[1234]

Pediatric Category	Age Range
Newborn (neonate)	Birth to 1 month of age
Infant	> 1 month to 2 years of age
Child	> 2 to 12 years of age
Adolescent	> 12 to 21 years of age

K. Proposed Labeling:

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

L. Conclusion:

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

[1] Mayo, Mayo Clinic – Mayo Medical Laboratories. Rochester 2014 Interpretive Handbook. 2014 Mayo Foundation for Medical Education and Research (MFMER).
[2] Lanzkowsky, Philip. *Pediatric Hematology-Oncology: a Treatise for the Clinician.* New York: McGraw-Hill, 1980.
[3] Nathan, David G. and Oski, Frank A. *Hematology of Infancy and Childhood.* 1987.
[4] Miller, Denis R., et al. *Blood Diseases of Infancy and Childhood.* St. Louis: Mosby, 1984.