DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Silver Spring, MD 20993-0002

September 1, 2016

Mindray Bio-medical Electronics Co., LTD
c/o Jinjie Hu, Ph.D.
Biologics Consulting Group
400 N. Washington St. Suite 100
Alexandria, VA 22314

Re: K160429
Trade/Device Name: BC-5390 Auto Hematology Analyzer
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated Differential Cell Counter
Regulatory Class: Class II
Product Code: GKZ
Dated: August 30, 2016
Received: August 31, 2016

Dear Dr. Hu:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Kelly Oliner -S

For
Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K160429

Device Name

BC-5390 Auto Hematology Analyzer

Indications for Use *(Describe)*

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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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510(K) SUMMARY

In accordance with 21 CFR 807.87(h) and (21 CFR 807.92) the 510(k) Summary for the BC-5390 Auto Hematology Analyzer is provided below.

Device Common Name:	Auto Hematology Analyzer
Device Proprietary Name:	BC-5390 Auto Hematology Analyzer
Submitter:	Mindray Bio-medical Electronics Co., LTD Mindray Building, Keji 12th Road South, High-tech Industrial Park, Nanshan, Shenzhen 518057, P.R. China
Contact:	Jinjie Hu Ph.D. 400 N. Washington Street Suite 100 Alexandria, VA 22314 Tel: 301-814-4985 Email: jhu@bcg-usa.com
Classification Regulation:	21 CFR 864.5220, Class II
Panel:	Hematology
Product Code:	GKZ

Predicate Device:

SYSMEX XE-2100 Automated Hematology Analyzer, K992875

Indication 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.

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 laboratory professionals to identify the normal patient, with all normal system-generated parameters, and to flag or identify patient results that require additional studies.

The BC-5390 Auto Hematology Analyzer system consists of:

- Instrument: Sample Processing Unit (SPU) and Data Managing Unit (DMU)
- Reagents
  M-53D DILUENT
  M-5LEO(I) LYSE
  M-5LEO(II) LYSE
  M-53LH LYSE
  PROBE CLEANSER
- Controls
  BC-5D Hematology Control (High, Normal, Low, Pending)
  Note: Controls for BC-5390 Auto Hematology Analyzer will be submitted in parallel with this 510(k) by R&D Systems as separate 510(k).
- Calibrator
  SC-CAL PLUS Hematology Calibrator (cleared as K955925)

The Analyzer provides analysis results of 21 parameters, 3 histograms and 1 scattergram of human blood. It supports two test panels: CBC and CBC+DIFF. The abbreviations for all parameters are listed in Table 1, Table 2 and Table 3.

Table 1: Parameters of BC-5390 Auto Hematology Analyzer

Analysis Parameter	Abbreviation	CBC	CBC + DIFF
White Blood Cell Count	WBC	√	√
Neutrophil Count	Neu#	/	√
Lymphocyte Count	Lym#	/	√
Monocyte Count	Mon#	/	√
Eosinophil Count	Eos#	/	√
Basophil Count	Bas#	/	√
Neutrophil Percent	Neu%	/	√
Lymphocyte Percent	Lym%	/	√
Monocyte Percent	Mon%	/	√
Eosinophil Percent	Eos%	/	√
Basophil Percent	Bas%	/	√
Red Blood Cell Count	RBC	√	√
Hemoglobin Concentration	HGB	√	√
Hematocrit	HCT	√	√
Mean Corpuscular Volume	MCV	√	√

Mean Corpuscular Hemoglobin	MCH	√	√
Mean Corpuscular Hemoglobin Concentration	MCHC	√	√
Red Blood Cell Distribution Width (Coefficient of Variation)	RDW-CV	√	√
Red Blood Cell Distribution Width (Standard Deviation)	RDW-SD	√	√
Platelet Count	PLT	√	√
Mean Platelet Volume	MPV	√	√

Table 2: Histograms of BC-5390 Auto Hematology Analyzer

Name	Abbreviation	CBC	CBC + DIFF
White Blood Cell/ Basophils Histogram	WBC/BASO Histogram	/	√
White Blood Cell Histogram	WBC Histogram	√	/
Red Blood Cell Histogram	RBC Histogram	√	√
Platelet Histogram	PLT Histogram	√	√

Table 3: Scattergram of BC-5390 Auto Hematology Analyzer

Name	Abbreviation.	CBC	CBC + DIFF
Differential Scattergram	Diff Scattergram	/	√

Comparison of Technological Characteristics:

The subject BC-5390 Auto Hematology Analyzer has similar technological characteristics, compared to the predicate device.

Both devices have similar intended uses as quantitative, automated hematology analyzers and leukocyte differential counters to be used in clinical laboratories for In-vitro Diagnostic purpose.

Safety testing was conducted on the subject BC-5390 Auto Hematology Analyzer per IEC 61010 and passed the standard requirement.

Substantial equivalence studies performed and demonstrated that the BC-5390 Auto Hematology Analyzer is similar to the predicate Sysmex XE-2100 (K992875).

Principle of Operation:

The patient whole blood sample or the prediluted sample with diluent is aspirated and delivered to the measuring bath to be measured. The measurement methods used in this analyzer are:

1. The Electrical Impedance method for determining the WBC/BAS, RBC and PLT by counting the electric pulses that occur in each cell size category. The BC-5390 Auto Hematology Analyzer determines the blood cell volume and identifies rare and pathological cells by creating and analyzing histograms of the various cell populations using their respective pulse data.
2. The colorimetric method is used for determining the Hemoglobin.
3. Flow Cytometry by laser is used to determine the WBC differential. When the blood cells suspended in the diluent pass through the flow cell, they are exposed to a laser beam. The intensity of scatter light reflects the blood cell size and intracellular density. A 2-dimensional distribution (scattergram) is drawn and analyzed to obtain the differential results.

Analysis Mode:

The BC-5390 provides the Closed Whole Blood Mode, Autoloader Whole Blood Mode and Closed Predilute Mode.

Test Panel:

The BC-5390 provides CBC and CBC+DIFF (CD) panels.

Specimen identification:

Specimen identification input is manual (by operator) or by barcode reader.

Specimen sampling and handling:

Samples are manually mixed and loaded into a sample compartment one at a time; or ten samples in a rack are automatically loaded, mixed and sampled for autoloader analysis. The BC-5390 processes anti-coagulated whole blood collected in a K_2EDTA or K_3EDTA on all modes.

Reagents, Calibrator and Controls

The details for reagents, calibrator and controls are presented below:

Reagents:

- M-53D DILUENT
- M-5LEO(I) LYSE
- M-5LEO(II) LYSE
- M-53LH LYSE

- PROBE CLEANSER

Controls: BC-5D Hematology Controls (High, Normal, Low) (K160606)

Three levels of Controls with low, normal and high levels are provided. It is recommended to perform the quality control check using these controls at intervals established by the laboratory procedures and local or national regulations.

Quality control performance was evaluated using BC-5D Hematology Controls.

Calibrator: SC-CAL PLUS Hematology Calibrator (cleared as K955925)

Calibration and verification of Calibration are performed with the previously cleared Calibrator SC-CAL PLUS Hematology Calibrator. The calibration and quality control should be performed according to the instruction for the Calibrator and to laboratory procedures and local or national regulations.

Software

The BC-5390 software system carries out the instrument function by taking the input information, triggering the functional modules, controlling and managing fluidic sequencing and measuring various blood cell parameters and recording the signals measured. Additionally, the software system also manages the counting results and sample information. Through its QA/QC program, the software system also provides daily maintenance functions. The software is designed to be intuitive user interface and to guide user workflows including error handling procedures. The software development processes and Hazard Analysis were conducted per FDA guidance.

Four Off-the-shelf (OTS) software products are used in BC-5390 (Windows 8.1 Professional 64bit, SQLite Database，Linux real-time operating system，Libxml2 Open Source file). The safety and effectiveness of the OTS software are assessed and verified in accordance with FDA Guidance “Guidance for Industry, FDA Reviewers and Compliance on Off-The-Shelf Software Use in Medical Devices, September 9, 1999”.Complete software documentation are submitted in accordance with Guidance “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices”, 2005.

Special Control and Guidances

Special Controls and Standard Guidance were used as references for the BC-5390 Auto Analyzer design, verification and validation studies. See Table 4 for the list of references.

Table 4: Special Control and Guidance Document Referenced

FDA Guidance	Class II Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells; Final Guidance for Industry and FDA	2001
H20-A2	Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard - Second Edition	2007
H26-A2	Validation, Verification and Quality Assurance of Automated Hematology Analyzers; Approved Standard—Second Edition	2010
EP05-A2	Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition	2004
EP6-A	Evaluation of the Linearity of Quantitative Measurement Procedure :A statistical Approach; Approved Guideline	2003
EP07-A2	Interference Testing in Clinical Chemistry-Approved Guideline—Second Edition	2005
EP09-A3	Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Third Edition	2013
EP28-A3c	Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition	2010
ICSH literature	ICSH guidelines for the evaluation of blood cell analysers including those used for differential leucocyte and reticulocyte counting. International Council for Standardization in Hematology. Int. Jnl. Lab. Hem. 2014, 36, 613-627	2014
EP25-A	Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.	2009
EP17-A	Protocols for Determination of Limits of Detection and Limits of Quantitation. Approved Guideline	2004

Performance Characteristics:

Method Comparison:

A total of 1531 whole blood samples (collected in K_2EDTA) were analyzed at three actual user sites. Five instruments and multiple operators were used for the study. The subjects of the study with age range from 1 day to 100 years old, and with 652 females and 874 males (5 subjects gender was not recorded). Patient's samples covered the normal and most abnormal conditions for all parameters. For each whole blood sample, three manual wedge smears were prepared and stained with Wright-Giemsa stain. A 400 cell WBC differential was performed on two smears per CLSI H20-A2. All samples were testing on whole blood mode in parallel with BC-5390 analyzer and the predicate device. An estimation of the bias was determined for each parameter (Exclude R). The result demonstrated the BC-5390 analyzer met the pre-defined specification for the difference limits. Whole blood accuracy and regression vs predicate and the flagging ability of BC-5390 vs Manual differential comparison were performed. The following tables showed that the results are comparable.

Table 5: The Correlation and Estimated Bias of BC-5390 (vs XE-2100, Combined)

Parameters	N	Result Range	r	slope (95%CI)	intercept (95%CI)
WBC	1091	0.06-177.15	0.999	1.006 (0.9903-1.021)	-0.07511 (-0.2123-0.06207)
Neu#	789	0.27-59.17	0.999	1.011 (0.9971-1.025)	-0.2916 (-0.09452-0.03620)
Lym#	864	0.00-9.68	0.993	0.9750 (0.9636-0.9863)	-0.01264 (-0.03416-0.008883)
Mon#	799	0.00-2.21	0.966	0.9303 (0.8912-0.9693)	0.02702 (0.01080-0.04324)
Eos#	932	0.00-3.39	0.995	0.9939 (0.9603-1.028)	9.386E-04 (-0.004361-0.006238)
Bas#	877	0.00-0.69	0.624	0.9156 (0.2266-1.605)	0.006836 (-0.006382-0.02005)
Neu%	792	19.6-99.6	0.995	0.9840 (0.9762-0.9919)	1.487 (0.9603-2.013)
Lym%	866	0.0-77.6	0.995	0.9897 (0.9814-0.9979)	-0.2723 (-0.4864--0.05818)
Mon%	792	0.20-16.40	0.930	0.9652 (0.9300-1.000)	0.2260 (0.03859-0.4134)
Eos%	936	0.00-37.40	0.994	0.9877 (0.9689-1.006)	0.02701 (-0.01416-0.06817)
Bas%	881	0.00-3.20	0.415	0.4308 (0.2936-0.5679)	0.2147 (0.1821-0.2472)
RBC	1451	1.13-7.75	0.997	1.004 (0.9999-1.008)	-0.001771 (-0.01777-0.01423)

Parameters	N	Result Range	r	slope (95%CI)	intercept (95%CI)
HGB	1486	3.30-23.1	0.998	1.010 (1.005-1.014)	-0.05500 (-0.1023-0.007685)
HCT	1452	10.50-67.80	0.995	1.013 (1.006-1.019)	-0.5671 (-0.7991-0.3351)
MCV	1452	53.70-127.10	0.993	1.036 (1.029-1.043)	-3.763 (-4.368--3.158)
MCH	1409	13.90-41.20	0.977	1.020 (1.008-1.032)	-0.5451 (-0.8854-0.2048)
MCHC	1408	23.80-37.70	0.825	1.184 (1.130-1.238)	-5.834 (-7.657-4.010)
RDW-CV	1453	11.10-29.70	0.978	1.024 (1.004-1.044)	-0.1895 (-0.4807-0.1018)
RDW-SD	1453	29.20-103.70	0.988	0.9878 (0.9760-0.9997)	-0.08935 (-0.6338-0.4551)
PLT	1199	4.00-1879.00	0.996	1.019 (1.012-1.026)	-1.157 (-2.215-0.1002)
MPV	1238	7.70-14.50	0.951	1.057 (1.037-1.078)	-0.7742 (-0.9964-0.5520)

The WBC Morphology flagging rate for the BC-5390 was compared to the WBC manual differential for the same population of samples as shown in table below.

Table 6: The WBC Morphology Flagging Ability of BC-5390 (vs Manual)

Flags	BC-5390
True Positive	283
True Negative	937
False Positive	260
False Negative	34
Total	1514
Sensitivity (TP %)	89.3%
Specificity (TN %)	78.3%
Efficiency	80.6%

Precision/Repeatability and Reproducibility

Repeatability study was conducted for each reported analyte parameter using whole blood samples collected in K_2EDTA anticoagulant tubes either with normal reference intervals or around medical decision levels. Each of the samples was tested 10 times consecutively within the same day of sample collection. Three analyzers in one clinical site with at least two professional laboratory technicians were used to conduct the studies. The SD and CV of the different parameters of those samples were calculated. The results met the predefined performance acceptance specifications.

Reproducibility study was conducted to verify the potential performance variation derived from testing sites, operator, reagent lots. Multiple lots reagent (five lots of Diluent, two lots of LH Lyse and LEO(II) lyse, and three lots of LEO(I) lyse), three BC-5390 Analyzers and two operators at each sites were used to conduct the study. Three levels of samples were prepared using commercial control material BC-5D and tested in duplicate for each run, twice each day for 20 days. A total of 80 (2 duplicates, 2 runs and 20 days) replicates for each sample were tested at each clinical site and 240 replicates together for all three sites for each level control. Standard deviation and CV% were calculated for each measurand and the results obtained were within the specifications.

Linearity Range

WBC and PLT high-value analogs, from commercialized materials, were diluted to different values to cover the AMR of WBC and PLT respectively. RBC/HGB linearity was performed using dilutions prepared from fresh whole blood. The whole blood was concentrated to obtain specimens to test the high linearity limit. Proportional dilutions were prepared using the diluent for each parameter to create 7 subsequent dilutions. The expected values of the diluted samples were considered the true values. Each level of the samples was run in triplicate. The mean of three runs from each of the 7 dilutions across the linear range were used. Acceptable performance is indicated by the data fitting a linear regression line with a coefficient of determination (R^2) of >0.95 and the parameters measured recovering within the bias limits for each parameters based on CLSI EP06-A. The results indicated that BC-5390 Auto Hematology Analyzer exhibits linearity across the claimed range.

Carryover

Carryover performance was determined for parameters WBC, RBC, HGB, HCT and PLT. Testing was performed based on the different analytical cycle combinations of within mode and mode to mode. For each analytical cycle combination, whole blood and predilute sample with extremely elevated blood components (high sample) and with decreased blood components (low sample) were tested in triplicates in turn according to H26-A2.

For whole blood and predilute sampling, within mode and mode to mode for sampling carryover was calculated and the results were within specifications (≤ 1.0%) for WBC, RBC, HGB, HCT and PLT. BC-5390 Analyzer demonstrated minimum carryover level within the defined specification for both Whole Blood and Predilute mode.

Interference

The potential interfering substances of BC-5390 were evaluated by measuring the whole blood samples and after adding different level of potential interfering substances. The paired difference testing was compared to the acceptance criteria. The impact of those substances were analyzed and the results demonstrated that there is no significant interference of bilirubin, WBC, and PLT for the results of BC-5390, but the high elevated concentration of Triglyceride (TG) and hemoglobin exhibits minor impact to the the HGB, MCH, MCHC parameters on the BC-5390. The information is disclosed in the BC-5390 Auto Hematology Analyzer Operator's Manual.

Other Compatibility Studies

Comparison of Whole Blood Mode and Predilute Mode

To demonstrate that BC-5390 analyzer performs equally on samples tested in different analysis modes (Whole blood and Predilute modes), 124 leftover whole blood samples representing the normal and medical conditions were collected in K_2EDTA collection tube. All the samples were tested in duplicate on BC-5390 analyzer with Closed or Autoloader Whole blood CD mode and Closed Predilute CD mode. The results were analyzed according to CLSI EP09-A3. It showed that there was no difference when testing samples in either mode or when the sample contained parameters in normal or abnormal range due to medical conditions.

Comparison of CBC and CBC+DIFF Mode

To demonstrate that BC-5390 analyzer performs equally on samples tested in different analysis modes (CBC and CBC+DIFF modes), 103 leftover whole blood samples representing the normal and medical conditions were collected in K_2EDTA collection tube for the comparison of Whole blood CBC and CD modes. Meanwhile, a total of 75 samples were collected in the same site for the comparison of Predilute CBC and CD modes. All the samples were tested in duplicate on BC-5390 analyzer with Closed or Autoloader Whole blood CD mode or Closed Predilute CD mode. The results were analyzed according to CLSI EP09-A3. It showed that there was no difference when testing samples in either mode or when the sample contained parameters in normal or abnormal range due to medical conditions.

Comparison of Capillary and Venous blood

To demonstrate the comparable performance between capillary and venous samples, 57 paired specimens were collected from donors by capillary method in K_2EDTA microtainers and venipuncture method in K_2EDTA collection tubes. Specimen levels were selected to cover the analytical measuring interval and medical decision levels for each parameter. Each sample was tested in the Closed whole blood CD mode at the U.S. site. The results were analyzed according to CLSI EP09-A3 and showed that the performance characteristics of the two specimen types were comparable.

Comparison of K_2EDTA and K_3EDTA Anticoagulants Samples

To evaluate whether samples collected in K_2EDTA and K_3EDTA have the same performance characteristics on BC-5390 analyzer, 70 paired fresh whole blood samples collected in K_2EDTA and K3EDTA anticoagulant tubes were tested. The samples were selected with the targets to cover the analytical measuring interval and medical decision levels for each parameter. Each sample was tested in Autoloader/Closed whole blood CD mode on BC-5390 in the clinical laboratory in U.S. The results were analyzed according to CLSI EP09-A3 and showed that the performance characteristics of the specimens collected in the two anticoagulants are comparable.

Sample Stability

Specimen stability study was conducted to support the specimen stability claim as for whole blood is 36 hours at refrigerated temperature (2-8°C) and 24 hours when stored at 18-26°C, and for predilute sample the stability is 25 minutes when stored at 18-26°C before testing. Fresh samples covering normal and medical decision range were stored at at 2-8°C and then tested at defined intervals of immediate (0-1hour), 4, 8, 12, 24, 26, 36 and 38 hours or stored at 18-26°C and then tested at the time points of immediate (0-1hour), 4, 8, 12, 14, 24 and 26 hours. Prediluted samples were also stored at 18-26°C and then tested at the time points of 5, 10, 15, 20, 25, 30, 35 minutes after sample preparation. The study results met the pre-defined acceptance criteria supporting the sample stability claims.

Reference Interval

A study was performed to assess the Adult Reference Ranges for BC-5390 analyzer using whole blood samples collected from 251 donors. In the study 121 adult male donors and 130 adult female donors between the ages of 19-70 were included. The non-parametric method and 95% confidence were used to calculate the lower and upper limits of the reference range according to EP28-A3c. The results are all shown in Table 7.

It is recommended that laboratories establish their own reference range based on the actual current patient population.

Table 7: The Reference Intervals of BC-5390

Parameters	Partitions*	Male			Female			Combined		
	(Female vs Male)	N	Low Limit (90%CI)	Upper Limit (90%CI)	N	Low Limit (90%CI)	Upper Limit (90%CI)	N	Low Limit (90%CI)	Upper Limit (90%CI)
WBC	YES	121	3.782 (3.560-4.000)	12.049 (11.420-12.580)	130	4.374 (4.130-5.000)	11.193 (10.380-11.850)	251	3.972 (3.780-4.330)	11.726 (11.120-12.060)
Neu#	NO	121	1.744 (1.460-2.050)	9.728 (7.870-9.780)	130	2.229 (2.060-2.580)	8.363 (7.230-8.690)	251	2.029 (1.740-2.190)	8.578 (7.860-9.280)
Lym#	NO	121	1.181 (1.150-1.400)	4.268 (3.220-4.920)	130	1.288 (0.920-1.460)	3.778 (3.410-4.110)	251	1.214 (1.150-1.400)	3.858 (3.430-4.280)
Mon#	YES	121	0.210 (0.150-0.250)	0.869 (0.780-0.920)	130	0.211 (0.160-0.240)	0.667 (0.630-0.710)	251	0.210 (0.160-0.240)	0.787 (0.710-0.870)

Parameters	Partitions*	Male			Female			Combined		
	(Female vs Male)	N	Low Limit (90%CI)	Upper Limit (90%CI)	N	Low Limit (90%CI)	Upper Limit (90%CI)	N	Low Limit (90%CI)	Upper Limit (90%CI)
Eos#	NO	121	0.031 (0.000-0.050)	0.599 (0.540-0.740)	130	0.023 (0.020-0.030)	0.487 (0.420-1.090)	251	0.030 (0.020-0.040)	0.557 (0.490-0.630)
Bas#	YES	121	0.010 (0.000-0.010)	0.100 (0.070-0.150)	130	0.010 (0.010-0.010)	0.080 (0.060-0.120)	251	0.010 (0.010-0.010)	0.080 (0.070-0.110)
Neu%	NO	121	39.06 (37.80-42.30)	78.14 (72.40-80.00)	130	41.94 (41.20-43.70)	76.49 (74.60-83.60)	251	41.33 (39.00-42.40)	76.90 (74.70-79.00)
Lym%	NO	121	14.13 (11.80-18.30)	50.47 (47.40-54.40)	130	16.14 (8.90-19.50)	49.67 (48.20-52.30)	251	15.13 (12.00-18.30)	49.84 (48.70-51.10)
Mon%	YES	121	3.61 (2.60-4.00)	10.90 (9.70-13.80)	130	3.63 (3.20-3.90)	8.87 (7.60-9.30)	251	3.63 (3.40-3.90)	9.77 (8.80-10.90)
Eos%	NO	121	0.41 (0.00-0.60)	8.82 (6.60-10.50)	130	0.40 (0.30-0.50)	8.12 (6.00-13.90)	251	0.40 (0.30-0.50)	8.10 (6.60-9.10)
Bas%	YES	121	0.20 (0.10-0.20)	1.20 (0.90-2.20)	130	0.20 (0.10-0.20)	1.00 (0.90-1.20)	251	0.20 (0.10-0.20)	1.10 (0.90-1.20)
RBC	YES	121	4.231 (3.660-4.370)	6.219 (6.000-6.380)	130	3.728 (3.540-4.010)	5.454 (5.310-5.940)	251	3.907 (3.660-4.130)	6.021 (5.920-6.220)
HGB	YES	121	13.01 (11.10-13.20)	18.28 (17.40-19.70)	130	10.18 (9.80-11.10)	16.27 (15.90-16.50)	251	10.68 (10.10-11.50)	17.47 (17.10-18.30)
HCT	YES	121	38.50 (34.60-39.20)	54.13 (51.40-56.70)	130	31.93 (31.70-34.30)	47.30 (46.70-48.70)	251	33.81 (31.90-35.40)	51.47 (50.60-54.20)
MCV	NO	121	74.28 (68.20-79.70)	100.68 (97.10-107.00)	130	74.33 (68.90-75.90)	96.87 (94.00-98.80)	251	74.33 (71.10-76.20)	97.64 (96.00-100.80)
MCH	NO	121	24.96 (22.90-26.60)	34.54 (32.80-36.50)	130	23.36 (22.40-25.10)	32.40 (31.90-34.50)	251	23.90 (22.90-25.10)	33.18 (32.40-34.60)
MCHC	YES	121	32.01 (30.10-32.50)	36.00 (35.80-36.20)	130	30.80 (29.40-31.40)	35.87 (35.20-36.10)	251	31.02 (30.30-31.90)	35.90 (35.70-36.10)
RDW-CV	YES	121	12.01 (11.90-12.30)	17.39 (15.80-18.50)	130	11.80 (11.50-12.10)	18.63 (17.50-20.50)	251	12.00 (11.80-12.20)	17.67 (17.20-18.90)
RDW-SD	NO	121	36.74 (35.20-37.90)	55.63 (51.30-58.30)	130	37.08 (34.50-39.10)	56.00 (52.60-57.90)	251	37.09 (35.90-38.00)	55.55 (52.60-57.70)
PLT	YES	121	141.1 (120.0-154.0)	456.6 (373.0-608.0)	130	186.4 (169.0-203.0)	405.5 (385.0-481.0)	251	147.7 (141.0-171.0)	435.4 (387.0-461.0)
MPV	NO	121	9.30 (9.10-9.40)	14.26 (13.00-15.90)	130	9.30 (9.20-9.40)	13.59 (12.70-14.20)	251	9.30 (9.20-9.40)	13.61 (12.90-14.30)

Note; * *in this table denoted that if significantly difference exists between Male and Female according to CLSI EP28-A3c. If noted "Yes", it indicated that a separate reference interval should be considered for the Male and Female.*

In addition, a literature reference interval verification study was performed in one clinical site for a total of 161 pediatric samples, including neonate (N=45), infant (N=26), child (N=57), and adolescent (N=33). These samples were collected from pediatric patients

ranging from neonates to 21 years of age. The results of this study verified the pediatric intervals published in Mayo and IOWA literature.

Please note, to substantiate a pediatric claim, we have included pediatric subjects in the method comparison and validated literature reference intervals according to FDA's recommendation in the pre-sub.

Determination of Limit of Blank (LoB), Limits of Detection (LoD) and Limit of Quantitation (LoQ)

Limit of Blank was determined using five blank samples (diluent) which just contain the dilute solution. To determine the Limits of Detection and Limit of Quantitation, five low levels of samples were created by adding whole blood samples to diluent to reach approximately 1-4 times of the LoB. Each blank sample or low level sample was tested 12 times at one clinical laboratory in the whole blood mode and predilute mode respectively on three BC-5390 analyzers. Each of the low level samples were tested 5 times on the Sysmex XE-2100 analyzer. The results were analyzed according to CLSI EP17-A. The maximum LoB, LoD, or LoQ value of the three (3) analyzers is taken as the reported value.

Substantial Equivalence

Table 8 and Table 9 summarize the similarities and differences between the BC-5390 Auto Hematology Analyzer and the predicate device XE-2100 Automated Hematology Analyzer.

Table 8: Device Comparison Table - Similarities

Similarities		
Item	**Subject Device BC-5390**	**Predicate XE-2100 (K992875)**
Overview layout		
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,	The Sysmex XE-2100 is a multi-parameter hematology analyzer intended to classify the following formed elements in anti-coagulated blood. WBC, Neut%/#, Lymph%/#, Mono%/#, Eos%/#, Baso%/#, NRBC%/# , RBC, HGB, HCT,

Similarities		
	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.	MCV, MCH, MCHC, RDW-CV, RDW-SD, RET%/#, IRF, PLT, MPV
Parameters	Parameters(21): WBC, Neu%, Lym%, Mon%, Eos%, Bas%, Neu#, Lym#, Mon#, Eos#, Bas#, RBC, HGB, HCT, MCV, MCH, MCHC, RDW-CV, RDW-SD, PLT, MPV	Same
Test Principle (RBC/PLT)	Impedance method	Same
Test Principle (HGB)	Colorimetric method	Same
Sample Type	Whole blood	Same
Sample Processing	Utilizes an automatic sampling, diluting and mixing device for sample processing	Same

Similarities		
Data Analysis	Raw data analyzed by algorithms to generate reported parameters	Same
Data Reporting	Display, printing and transmission of data to LIS/HIS.	Same
Sample ID	Manual or Automatic barcode scan of sample tube identifier or manual keyboard entry of sample identifier	Same
Software Risk Level	Moderate	Same
I/O Interfaces	One LAN interface	Same
Software	DMU (Data Management Unit) Function: Managing data, such as editing worklist, reviewing results, generating reports, communicating with LIS/HIS, etc.	IPU (Information Processing Unit) Function: Same

Table 9: Device Comparison Table - Differences

Differences		
Item	**Device BC-5390**	**Predicate XE-2100 (K992875)**
Parameters (Reticulocytes, Nucleated RBC)	Not Available	RET%/#, IRF, NRBC%/#
Reagents	M-53D DILUENT M-5LEO(I) LYSE M-5LEO(II) LYSE M-53LH LYSE PROBE CLEANSER	CELLPACK, CELLSHEATH STROMATOLYSER-4DS STROMATOLYSER-4DL STROMATOLYSER-FB, SULFOLYSER CELLCLEAN

Differences		
Item	**Device BC-5390**	**Predicate XE-2100 (K992875)**
		Plus Reagents with IMI, RET, NRBC (STROMATOLYSER-NR, STROMATOLYSER-IM, RET-SEARCH II)
Test Panel	CBC CBC+DIFF	Same Plus RET and NRBC
Test Principle (WBC)	WBC: Flow Cytometry by Laser and Electrical Impedance Method	WBC: Flow Cytometry method using semiconductor laser detection method
Throughput	Closed Whole Blood Mode: Upper capacity of 51 samples/hour Autoloader Whole Blood Mode: Upper capacity of 60 samples/hour Closed Predilute Mode: Upper capacity of 53 samples/hour	CBC, CBC+DIFF: Approx. 150 samples/hour Mode with NRBC, RET: Approx. 113-150 samples/hour
Sample Volume	Autoloader Whole Blood Mode and Closed Whole Blood Mode：33μL Closed Predilute Mode：20μL	Closed and Sampler Mode: Approx. 200μL Manual Mode: Approx. 130μL Capillary Mode: 40μL
Sample assignment mechanism	Using the sample assignment Syringe to assign the sample to the baths in sequence	Using the sample rotary valve (SRV) to assign the sample to the baths simultaneously
Drive Source Unit	Pump	Pneumatic unit
Analysis Mode	Closed Whole Blood Mode Autoloader Whole Blood Mode Closed Predilute Mode	Closed Mode Autoloader Mode Predilute Mode and Manual Mode
Sample Anticoagulant	K_2EDTA or K_3EDTA	K_2EDTA or K_3EDTA And EDTA-2Na

Differences		
Item	**Device BC-5390**	**Predicate XE-2100 (K992875)**
Controls	BC-5D Hematology Control – 3 Levels of High, Normal and Low	e-CHECK – 3 Levels
Calibrator	SC-CAL PLUS Hematology Calibrator	SCS-1000 Calibrator
Quality Control Techniques	L-J QC Program X-B QC Program	L-J QC Program X-M QC Program
Data Storage	Analysis data with histograms and scattergrams: 100,000 samples Patient information: 100,000 persons Order information: 4,000 samples Quality control (QC) files: 60 files	Analysis data with histograms and scattergrams: 10,000 samples Patient information: 5,000 persons Order information: 1,000 samples Quality control (QC) files: 20 files

Substantial Equivalence Conclusion

The BC-5390 Auto Hematology Analyzer has the same intended use as the predicate device, the XE-2100 as cleared in K992875. They are the quantitative, automated hematology analyzer and leukocyte differential counter for In Vitro Diagnostic Use in clinical laboratories. These analyzers may be used in adult and pediatric population. Both analyzers are only to be used by trained laboratory 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 of 21 parameters of human blood, 3 histograms and 1 scattergram. The performance comparison study results demonstrated that the BC-5390 Auto Hematology Analyzer is substantially equivalent to the predicate device, the XE-2100 Automated Hematology Analyzer (K992875) and the differences do not raise new questions of the safety and effectiveness.