

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

A. 510(k) Number:

K181475

B. Purpose for Submission:

Clearance of a new device

C. Manufacturer and Instrument Name:

Beckman Coulter DxH 520 Hematology Instrument

D. Type of Test or Tests Performed:

Complete blood count and 5-part leukocyte differential: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, LY%, LY#, MO%, MO#, NE%, NE#, EO%, EO#, BA%, and BA# parameters.

E. System Descriptions:

1. Device Description:

The DxH 520 instrument system is comprised of the analyzer, software, and reagents that allow for quantitative determination of hematological measurements through the use of impedance, spectrophotometry, and optical technology. Additional reagents provide system cleaning, quality control and calibration. The system includes the following reagents :

- DxH 500 series Lyse – a cyanide-free, aldehyde-free erythrocyte lytic agent for the quantitative determination of hemoglobin, dilution for the classification of WBC subpopulations, and counting leukocytes.
- DxH 500 Series Diluent – an aldehyde-free, isotonic-buffered saline solution that is used to dilute the specimen and used to rinse module components between sample analyses.
- DxH 500 Series Cleaner – a cyanide-free, aldehyde-free cleaning agent for components that come in contact with blood samples to remove residual material from the system.

2. Principles of Operation:

Measurement of Hemoglobin

Using the DxH 520 hemoglobin reagent (DxH 500 Series Lyse), the hemoglobin derivatives are stabilized in an oxyhemoglobin ferrous form. The resulting complex is then measured by spectrophotometry using a LED $\lambda=545\text{nm}$ with a $\delta\lambda=40\text{nm}$ (+/- 20nm bandwidth).

Determination of Count/Size for White Blood Cells, Red Blood Cells and Platelets

The Coulter Principle (impedance) is used to count and size cells by detecting and measuring changes in electrical resistance when a particle (such as a cell) in a conductive liquid passes through a small aperture. Platelet counting and sizing are performed in the RBC bath. Thresholds separate the platelet pulses, which are much smaller than the RBC pulses.

RBC and PLT Histograms

Red blood cells (RBCs) are categorized by size (volume) and plotted on a size distribution curve to form the RBC histogram. Platelets are also categorized according to size to develop a size distribution curve of the particles.

Leukocyte 5-Part Differential

The leukocyte 5-part differential is determined by using the simultaneous measurement of impedance and direct optical measurement (Axial Light Loss - ALL) using a blue LED focused through the WBC aperture.

3. Modes of Operation:

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes ☒ or No ☐

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

Yes ☐ or No ☒

4. Specimen Identification:

Specimen identification is performed by manual entry using a keyboard or hand-held barcode reader.

5. Specimen Sampling and Handling:

Whole blood specimens are processed using a closed-vial sampling method as default with the option to run in open-vial mode if selected by the operator. For open-vial

sampling, the whole blood specimen (single tube) is to be manually mixed and presented to the analyzer by the operator.

6. Calibration:

The DxH 500 Series Calibrator is intended for the determination of CBC calibration factors (WBC, RBC, HGB, MCV, PLT and MPV). The calibrator is comprised of human and animal cells to simulate human blood cell populations.

7. Quality Control:

The DxH 500 Series Control is a hematology tri-level (low, normal and high) quality control material intended to monitor the system's performance for the CBC and 5-part differential parameters. The calibrator is comprised of human and animal cells to simulate human blood cells.

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 DxH 520 is a quantitative, multi-parameter, automated hematology analyzer for in

vitro diagnostic use in clinical laboratories and physician's office laboratories. It is used to identify the normal patient with normal system-generated parameters from patients with abnormal parameters and/or flags that require additional studies.

The DxH 520 identifies and enumerates the following parameters: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, LY%, LY#, MO%, MO#, NE%, NE#, EO%, EO#, BA%, BA# in whole blood samples (venous and capillary) collected in K₂EDTA and K₃EDTA anticoagulants, and prediluted whole blood.

The instrument is for use in adult and pediatric populations, including neonates.

LIMITATIONS

All numerical results reported for Basophil count and percent values must be reflexed for manual microscopy or followed up for additional testing based on the laboratory's SOP.

2. Special Conditions for Use Statement(s):

For prescription use only

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:

UniCel® DxH 800 COULTER Cellular Analysis System; K120771, K140911

2. Comparison with Predicate Device:

Similarities		
Item	Device DxH 520	Predicate UniCel® DxH 800
Intended Use	The DxH 520 is a quantitative, multi-parameter, automated hematology analyzer for in vitro diagnostic use in clinical laboratories and physician's office laboratories. It is used to identify the normal patient with normal system-generated parameters from patients with abnormal parameters and/or flags that require additional studies. The DxH 520 identifies and enumerates the following parameters: WBC, RBC, HGB,	The UniCel® DxH 800 Analyzer is a quantitative multi-parameter, automated hematology analyzer for in vitro diagnostic use in screening patient populations found in clinical Laboratories. The UniCel® DxH 800 Analyzer identifies and enumerates the parameters indicated below on the following sample types: • Whole Blood (Venous and Capillary)

Similarities		
Item	Device DxH 520	Predicate UniCel® DxH 800
	HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, LY%, LY#, MO%, MO#, NE%, NE#, EO%, EO#, BA%, BA# in whole blood samples (venous and capillary) collected in K2EDTA and K3EDTA anticoagulants, and prediluted whole blood. The instrument is for use in adult and pediatric populations, including neonates. LIMITATIONS All numerical results reported for Basophil count and percent values must be reflexed for manual microscopy or followed up for additional testing based on the laboratory's SOP.	WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, NE%, NE#, LY%, LY#, MO%, MO#, EO%, EO#, BA%, BA#, NRBC%, NRBC#, RET%, RET#, MRV, IRF • Pre-Diluted Whole Blood (Venous and Capillary) WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDWSD, PLT, MPV • Body Fluids (cerebrospinal, serous and synovial) TNC and RBC
WBC, RBC, MCV, Platelet measurement	Aperture impedance (Coulter® Principle)	same
Hemoglobin measurement	Spectrophotometric	same
Data reporting	Display of graphics, hardcopy printing and transmission to Laboratory Information System (LIS)	same

Differences		
Item	Device DxH 520	Predicate UniCel DxH 800
5-Part Differential	Optical / Impedance • Aperture impedance (DC) • Light Absorbance (LED) – Axial Light Lost	VCSn Technology using : • Aperture impedance (DC) • Conductivity (RF) • Laser Light Scatter (Multiple angles) • Laser Light Absorbance
Reagents	DxH 500 Series Diluent DxH 500 Series Lyse DxH 500 Series Cleaner	COULTER DxH Diluent COULTER DxH Diff Pack COULTER DxH Cell Lyse

Differences		
Item	Device DxH 520	Predicate UniCel DxH 800
		COULTER DxH Retic Pack COULTER DxH Cleaner
Quality Controls & Calibrator	DxH 500 Series Control DxH 500 Series Calibrator DXH 500 Linearity Kit	COULTER 6C Cell Control COULTER Latron CP-X Control COULTER RETIC-X Cell Control COULTER LIN-X Control COULTER Body Fluids Control COULTER S-CAL Calibrator kit
System Configuration	• Bench top only • Integrated single board computer with color touch screen running application specific software using Linux OS • Handheld Barcode Scanner • Printer	• Bench top or Optional Floor Stand - provides self-contained support for the analyzer as well as easy access storage for reagents and waste containers • PC based workstation running Microsoft Windows XP application specific software • Handheld Barcode Scanner • Printer
Sampling Mechanism	Manual single tube presentation in closed-vial and open-vial sampling modes	Manual single tube presentation in closed-vial and open-vial sampling modes Automated closed-vial presentation with a 5-position cassette (maximum initial load capacity is 20 racks)
Sample Aspiration Volume	Manual single tube presentation in closed-vial and open-vial sampling modes: 16.7 µL Pre-dilute mode: 20µL whole blood + 300 µL diluent	Automatic cap-piercing: 165 µL Single tube - open-vial and cap pierce: 165 µL Pre-dilute 165 µL - fixed ratio of 1 in 5 dilution of blood with diluent
Throughput	Closed-vial sampling mode: 55	Automated cassette processing-

Differences		
Item	Device DxH 520	Predicate UniCel DxH 800
	samples per hour Open-vial sampling mode: 60 samples per hour	CBC ≥ 100 specimens per hour CBC/Diff ≥ 100 specimens per hour CBC/Diff/NRBC ≥ 90 specimens per hour Any cycle with Retic ≥ 45 specimens per hour
Controlling Software	The software is specific for the (DxH 500 and 520 analyzers) and runs on an integrated single board computer with color touch screen using Linux OS. The software provides all functions required for the User Interface, Data analysis, Results management, Instrument control and monitoring.	The software (embedded and workstation) is specific to support all features of the DxH 800. The software system consists of a Data Manager component, a System Manager component (including algorithms), the User Interface, all of which are resident in the Workstation. The Embedded Application, which is resident in the analyzer, uploads from the workstation on system power-up.

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

CLSI C56-A, Hemolysis, Icterus, and Lipemia/Turbidity Indices as Indicators of Interference in Clinical Laboratory Analysis; Approved Guideline July 2012. FDA Recognition Number 7-242.

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition, October 2014. FDA Recognition Number 7-251.

CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; 1st Edition. Approved Guideline. FDA Recognition Number 7-193.

CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition. FDA Recognition Number 7-127.

CLSI EP12-A2, User Protocol for Evaluation of Qualitative Test Performance; Approve Guideline. Second Edition. FDA Recognition Number 7-152.

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory measurement Procedures; Approved Guideline-second Edition. June 2012. FDA Recorgnition Number 7-233

CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents, 1st Edition. FDA Recognition Number 7-235.

CLSI EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition, October 2010. FDA Recorgnition Number 7-224.

CLSI GP41-A6, Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard-Sixth Edition. October 2007. FDA Recognition Number 7-201.

CLSI GP42-A6, Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard-Sixth Edition. September 2008. FDA Recognition Number 7-203.

CLSI H20-A2, Reference Leukocyte (WBC) Differential Count (proportional) and Evaluation of Instrumental Methods; Second Edition, 2007. FDA Recorgnition Number 7-165.

CLSI H26-A2, Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard - Second Edition, June 2010. FDA Recorgnition Number 7-210.

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; December 4, 2001.

Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests; Final Guidance for Industry and FDA Staff; March 2007.

J. Performance Characteristics:

1. Analytical Performance:

a. Method Comparison

The method comparison studies were performed at six sites (three clinical laboratories and three physician office laboratories—also referred to as POLs) to compare the performance of the DxH 520 Hematology Instrument to the UniCel DxH 800 COULTER Cellular Analysis System using a total of 688 residual whole blood samples collected in K₂EDTA anticoagulant collection tubes. Venous (n=600) and capillary (n=88) whole blood samples were analyzed in the open- and closed-vial

sampling modes. The study included pediatric (neonate to ≤ 21 years) and adult subjects with the following conditions: anemia, thrombocytosis, sickle cell anemia, acute lymphoblastic leukemia, acute myeloid leukemia, chronic myelomonocytic leukemia, chronic lymphoblastic leukemia (CLL), chronic myeloblastic leukemia (CML), pancytopenia, polycythemia, lymphoma, multiple myeloma, infection and human immunodeficiency virus (HIV).

Deming regressions were used to estimate the regression models (i.e. slope, intercept, 95% confidence intervals (CI) and correlation coefficient (r)). Bland-Altman (difference) plots and 95% limits of agreement (LOA) were presented to show the average of the test and reference value on the X-axis and the difference between the test and the reference methods on the Y-axis. Bias at medical decision points were also evaluated for each site and for all sites combined. All results were within the pre-defined acceptance criteria and found to be acceptable with the exception of the basophil parameters.

All sites combined - Regression Analysis

Parameter	Mean	Slope (95% CI)	Intercept (95% CI)	(r)
WBC (10^3 cells/uL)	10.242	1.000 (0.996, 1.004)	0.038 (0.026, 0.051)	0.999
RBC (10^6 cells/uL)	4.242	1.013 (1.007, 1.018)	-0.009 (-0.029, 0.01)	0.996
HGB (g/dL)	12.528	1.027 (1.02, 1.033)	-0.179 (-0.259, -0.099)	0.996
HCT (%)	37.24	0.995 (0.986, 1.005)	0.252 (-0.078, 0.583)	0.993
MCV (fL)	88.943	0.998 (0.985, 1.012)	-0.529 (-1.697, 0.639)	0.99
MCH (pg)	29.872	0.940 (0.924, 0.956)	1.798 (1.341, 2.254)	0.981
MCHC (g/dL)	33.566	0.931 (0.857, 1.006)	2.574 (0.1, 5.049)	0.735
RDW (%)	15.339	0.918 (0.884, 0.953)	1.095 (0.587, 1.603)	0.938
RDW-SD (fL)	47.334	0.923 (0.885, 0.962)	3.463 (1.699, 5.228)	0.941
PLT (10^3 cells/uL)	279.844	0.998 (0.984, 1.012)	-1.132 (-3.426, 1.161)	0.992
MPV (fL)	9.146	1.09 (1.016, 1.165)	-0.591 (-1.227, 0.045)	0.801
LY (%)	27.321	0.981 (0.964, 0.998)	1.179 (0.768, 1.589)	0.995

Parameter	Mean	Slope (95% CI)	Intercept (95% CI)	(r)
#LY (10 ³ cells/uL)	2.253	1.01 (1.002, 1.018)	0.042 (0.036, 0.049)	0.998
MO (%)	8.501	0.949 (0.913, 0.984)	0.171 (-0.149, 0.49)	0.968
#MO (10 ³ cells/uL)	0.693	0.976 (0.958, 0.993)	-0.002 (-0.009, 0.005)	0.637
NE (%)	61.085	0.996 (0.989, 1.004)	0.085 (-0.407, 0.577)	0.996
#NE (10 ³ cells/uL)	5.386	1.000 (0.987, 1.012)	0.002 (-0.026, 0.029)	0.997
EO (%)	2.807	0.987 (0.958, 1.015)	0.265 (0.195, 0.336)	0.967
#EO (10 ³ cells/uL)	0.211	1.007 (0.976, 1.037)	0.015 (0.009, 0.021)	0.985
BA (%)	0.316	0.076 (0.015, 0.137)	0.262 (0.218, 0.306)	0.215
#BA (10 ³ cells/uL)	0.028	0.499 (0.453, 0.544)	0.002 (0.002, 0.003)	0.507

A total of 424 samples were used from three test sites to provide an assessment of the overall flagging capability of the DxH 520 instrument against the reference method (manual light microscopy). The study was conducted by two operators performing a 200 cell count differential. The false positive (FP) rate, false negative (FN) rate, sensitivity/specificity and negative predictive value/positive predictive value were determined and are presented in the tables below for distributional flagging, morphology flagging and all flagging combined.

Statistic	Distributional	Morphology	All Flagging
	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)
Sensitivity	83.8% (78.1, 88.3)	80.6% (70.0, 88.0)	86.5% (81.4, 90.4)
Specificity	69.5% (63.2, 75.1)	78.4% (73.8, 82.4)	68.7% (61.9, 74.7)
PPV	70.6% (64.5, 76.1)	43.3% (35.2, 51.7)	75.4% (69.8, 80.3)
NPV	83.1% (77.1, 87.7)	95.2% (92.1, 97.1)	82.1% (75.7, 87.2)
FP	30.5% (24.9, 36.8)	21.6% (17.6, 26.2)	31.3% (25.3, 38.1)
FN	16.2% (11.7, 21.9)	19.4% (12.0, 30.0)	13.5% (9.6, 18.6)

b. Precision/Reproducibility:

To evaluate precision and reproducibility, studies were conducted in clinical laboratories and POL sites.

Repeatability

The repeatability study was conducted at multiple clinical laboratory sites using multiple operators and multiple DxH 520 analyzers over multiple operating days. A total of 112 samples residual native whole blood samples collected in K₂EDTA collection tubes were selected within the defined ranges and around medical decision points per the CLSI H26-A2 standard. Each sample was analyzed 10 consecutive times in the closed-vial sampling mode. All results met the predefined acceptance criteria and were determined to be acceptable.

To evaluate operator variability at POL sites, a repeatability study was conducted in whole blood closed-vial mode and the pre-dilute testing mode using 24 residual samples. Whole blood samples were analyzed by each operator for 10 replicates (each sample) analyzed in the closed-vial mode. Pre-diluted samples were also analyzed by each operator in the pre-dilute mode for 10 replicates. Samples were tested by two or three operators at the POL sites. All results met the predefined acceptance criteria and were determined to be acceptable.

Reproducibility

To evaluate reproducibility at clinical laboratory sites, three different levels of quality control materials (low, normal, high) were used. The same lot was tested across all sites. Control vials were run in duplicate twice each day for a minimum of 20 days at one site and in triplicate twice each day for five days at the other two sites. All results met the predefined acceptance criteria and were determined to be acceptable.

To evaluate reproducibility at POL sites, one lot of quality control material (low, normal, high) was run once a day across three sites for five days with five replicates for each QC level. The data generated from this assessment was used to calculate repeatability (within-run precision), between-day and between-site, and reproducibility (total precision). For each reported parameter and for each level of control tested, the sample size (N), mean, SD and %CV of the various components of precision were calculated along with the 95% CI of the SD and %CV for repeatability and reproducibility (total precision). All results met the predefined acceptance criteria and were determined to be acceptable.

Combined POL Sites (low level control)

Parameter	N	Mean	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC (10 ³ cells/uL)	79	2.41	0.044	1.81	0.024	0.99	0.030	1.22	0.058	2.40

Parameter	N	Mean	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
RBC (10 ⁶ cells/uL)	79	2.50	0.029	1.16	0.014	0.55	0.031	1.24	0.045	1.79
HGB (g/dL)	79	6.77	0.054	0.80	0.044	0.65	0.047	0.70	0.084	1.25
HCT (%)	79	19.76	0.227	1.15	0.180	0.91	0.000	0.00	0.290	1.47
MCV (fL)	79	79.02	0.226	0.29	0.476	0.60	1.125	1.42	1.242	1.57
MCH (pg)	79	27.08	0.296	1.09	0.177	0.65	0.105	0.39	0.361	1.33
MCHC (g/dL)	79	34.28	0.358	1.05	0.303	0.88	0.288	0.84	0.550	1.61
RDW (%)	79	13.59	0.139	1.03	0.160	1.18	0.178	1.31	0.277	2.04
RDW-SD	79	41.96	0.616	1.47	0.000	0.00	1.104	2.63	1.264	3.01
PLT (10 ³ cells/uL)	79	77.84	3.756	4.83	1.327	1.70	2.093	2.69	4.500	5.78
MPV (fL)	79	9.87	0.249	2.52	0.112	1.14	0.000	0.00	0.273	2.76
LY (%)	79	43.16	1.077	2.50	0.486	1.13	1.119	2.59	1.628	3.77
#LY (10 ³ cells/uL)	79	1.04	0.031	3.02	0.023	2.17	0.039	3.78	0.055	5.31
MO (%)	79	2.11	0.303	14.37	0.058	2.76	0.000	0.00	0.309	14.63
#MO (10 ³ cells/uL)	79	0.05	0.007	14.35	0.003	5.21	0.001	2.18	0.008	15.43
NE (%)	79	43.36	1.096	2.53	0.000	0.00	1.182	2.73	1.612	3.72
#NE (10 ³ cells/uL)	79	1.05	0.033	3.13	0.000	0.00	0.014	1.31	0.035	3.39
EO (%)	79	11.31	0.824	7.29	0.386	3.41	0.000	0.00	0.909	8.04
#EO (10 ³ cells/uL)	79	0.27	0.022	7.98	0.008	2.84	0.003	1.16	0.023	8.55
BA (%)	79	0.06	0.054	84.06	0.000	0.00	0.004	6.84	0.054	84.34
#BA (10 ³ cells/uL)	79	0.00	0.002	624.45	0.000	0.00	0.000	0.00	0.002	624.45

Combined POL sites (normal level control)

Parameter	N	Mean	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC (10 ³ cells/uL)	82	7.37	0.103	1.39	0.067	0.91	0.118	1.60	0.170	2.31

Parameter	N	Mean	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
RBC (10 ⁶ cells/uL)	82	4.73	0.053	1.11	0.026	0.55	0.050	1.06	0.077	1.63
HGB (g/dL)	82	14.51	0.117	0.81	0.073	0.50	0.166	1.14	0.216	1.49
HCT	82	41.01	0.452	1.10	0.395	0.96	0.000	0.00	0.601	1.46
MCV (fL)	82	86.69	0.236	0.27	0.441	0.51	0.644	0.74	0.816	0.94
MCH (pg)	82	30.67	0.254	0.83	0.036	0.12	0.000	0.00	0.257	0.84
MCHC (g/dL)	82	35.38	0.284	0.80	0.225	0.63	0.281	0.80	0.458	1.30
RDW (%)	82	12.98	0.128	0.98	0.111	0.85	0.109	0.84	0.201	1.55
RDW-SD (fL)	82	45.39	0.551	1.21	0.000	0.00	0.911	2.01	1.065	2.35
PLT (10 ³ cells/uL)	82	253.1 5	7.563	2.99	6.282	2.48	11.181	4.42	14.889	5.88
MPV (fL)	82	8.87	0.104	1.17	0.096	1.08	0.072	0.81	0.159	1.79
LY (%)	82	27.81	0.653	2.35	0.199	0.72	0.739	2.66	1.006	3.62
#LY (10 ³ cells/uL)	82	2.05	0.057	2.78	0.030	1.45	0.088	4.28	0.109	5.31
MO (%)	82	1.91	0.188	9.84	0.000	0.00	0.106	5.55	0.216	11.30
#MO (10 ³ cells/uL)	82	0.14	0.014	10.00	0.000	0.00	0.010	7.19	0.017	12.31
NE (%)	82	66.07	0.672	1.02	0.224	0.34	1.170	1.77	1.367	2.07
#NE (10 ³ cells/uL)	82	4.87	0.080	1.65	0.039	0.80	0.049	1.01	0.102	2.09
EO (%)	82	4.16	0.250	6.03	0.118	2.85	0.732	17.61	0.783	18.83
#EO (10 ³ cells/uL)	82	0.31	0.019	6.35	0.009	3.01	0.054	17.75	0.059	19.09
BA (%)	82	0.05	0.030	56.56	0.000	0.00	0.017	32.09	0.034	65.02
#BA (10 ³ cells/uL)	82	0.00	0.004	129.10	0.000	0.00	0.003	85.30	0.005	154.73

Combined POL sites (high level control)

Parameter	N	Mean	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC (10 ³ cells/uL)	80	18.20	0.179	0.98	0.064	0.35	0.135	0.74	0.233	1.28

Parameter	N	Mean	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
RBC (10 ⁶ cells/uL)	80	5.24	0.056	1.07	0.033	0.63	0.059	1.13	0.088	1.68
HGB (g/dL)	80	17.69	0.114	0.64	0.041	0.23	0.204	1.15	0.237	1.34
HCT (%)	80	49.47	0.516	1.04	0.457	0.92	0.181	0.37	0.713	1.44
MCV (fL)	80	94.39	0.227	0.24	0.390	0.41	0.813	0.86	0.929	0.98
MCH (pg)	80	33.75	0.268	0.79	0.185	0.55	0.103	0.31	0.342	1.01
MCHC (g/dL)	80	35.77	0.272	0.76	0.292	0.82	0.206	0.58	0.449	1.26
RDW (%)	80	11.98	0.132	1.10	0.093	0.77	0.139	1.16	0.213	1.78
RDW-SD (fL)	80	46.00	0.567	1.23	0.133	0.29	1.141	2.48	1.281	2.78
PLT (10 ³ cells/uL)	80	507.27	12.905	2.54	6.360	1.25	16.375	3.23	21.797	4.30
MPV (fL)	80	8.67	0.082	0.94	0.035	0.40	0.000	0.00	0.089	1.02
LY (%)	80	13.18	0.298	2.26	0.000	0.00	0.416	3.15	0.512	3.88
#LY (10 ³ cells/uL)	80	2.40	0.053	2.23	0.010	0.42	0.095	3.96	0.109	4.56
MO (%)	80	2.23	0.124	5.57	0.041	1.85	0.141	6.32	0.192	8.63
#MO (10 ³ cells/uL)	80	0.41	0.024	6.01	0.007	1.70	0.028	6.79	0.037	9.23
NE (%)	80	76.17	0.411	0.54	0.052	0.07	0.885	1.16	0.977	1.28
#NE (10 ³ cells/uL)	80	13.86	0.161	1.16	0.065	0.47	0.075	0.54	0.189	1.37
EO (%)	80	8.39	0.272	3.25	0.124	1.47	0.675	8.05	0.739	8.81
#EO (10 ³ cells/uL)	80	1.53	0.052	3.43	0.017	1.10	0.128	8.37	0.139	9.11
BA (%)	80	0.03	0.015	42.86	0.005	13.91	0.010	29.72	0.019	53.98
#BA (10 ³ cells/uL)	80	0.01	0.004	49.12	0.001	15.60	0.003	37.73	0.005	63.87

c. *Linearity:*

Linearity was assessed by demonstrating that the reported results were directly proportional to the concentration of the measurand in a test sample for the WBC, RBC, HGB and PLT parameters. The linearity study was performed using three

instruments.

Regression analysis was used to assess linearity for the first-order model (e.g. linear), and weighted polynomial regression was used to assess linearity for the second- and third-order models (e.g. quadratic and cubic). WBC, PLT and HGB achieved linearity with a first-order model whereas RBC linearity was achieved through polynomial regression (third order model).

Parameter	Measuring Range
WBC (10^3 cells/uL)	0.20–100.0
RBC (10^6 cells/uL)	0.20–8.0
HGB (g/dL)	0.20–25.0
PLT (10^3 cells/uL)	7.0–2000.0

d. Carryover:

Carryover studies for the WBC, RBC, HGB, and PLT parameters were conducted at three sites in the closed-vial sampling mode. Fresh and contrived whole blood samples were used to create high target value (HTV) samples for WBC and HGB. Diluent was used for low target value (LTV) sample. Testing was performed on four instruments. Each HTV sample was analyzed in triplicate, followed by three aspirations of a LTV sample. The results of the carryover study were within the pre-defined acceptance criteria and were determined to be acceptable for each parameter tested.

e. Interfering Substances:

The interference effect of hemolysis, lipemia, icterus (unconjugated or conjugated bilirubin), high levels of WBCs ($100 \times 10^3/\mu\text{L}$) and high levels of platelets ($\text{PLT} > 1000 \times 10^3/\mu\text{L}$) were evaluated in the interference study. For lipemia, seven concentrations were analyzed in five replicates. For hemolysis, icterus and high levels of WBCs, test concentrations selected from the CLSI EP07-A2 guideline were analyzed in ten replicates. The concentrations indicated in the table below for lipemia, conjugated bilirubin, unconjugated bilirubin, and hemoglobin are the highest concentrations that did not interfere with the following parameters: WBC, RBC, HGB, HCT, MCV, MCHC, RDW, RDW-SD, PLT and MPV. For high levels of platelets (as an interferent), the following parameters were evaluated: WBC, RBC, HGB, PLT and MPV. For high levels of WBCs (as an interferent), the HGB parameter was evaluated.

Test Case	Results
Dose Response and Interference Confirmation: Lipemia	62.5 mg/dL

Test Case	Results
Interference Confirmation: Conjugated Bilirubin	40mg/dL
Interference Confirmation: Unconjugated Bilirubin	20mg/dL
Interference Confirmation: Hemoglobin	200 mg/dL
Interference Confirmation: Leukocytes	100 x10 ³ /uL
Interference Confirmation:Platelets	2000 x 10 ³ /μL

2. Other Supportive Instrument Performance Data Not Covered Above:

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

Studies were conducted to evaluate LoB, LoD and LoQ for the WBC, RBC, HGB and PLT parameters on the DxH 520 Hematology Analyzer. The study was conducted using three DxH 520 instruments and two reagent lots. To determine LoB, testing was performed on three individual test days, with 40 runs per day using diluent as a test sample for each DxH 520 instrument yielding a total of 120 measurements/instrument. To determine limit of detection (LoD) and limit of quantitation (LoQ), four samples per parameter were evaluated. Three sets of 11 dilutions of the stock solution were prepared. Five replicates of each dilution level was analyzed on each test instrument. The LoD and LoQ study was carried out over two days on the same three instruments. The LoB, LoD and LoQ were determined as follows.

Parameter	LoB	LoD	LLoQ
WBC	0.020	0.032	0.072
RBC	0.010	0.014	0.044
HGB	0.010	0.040	0.123
PLT	1.700	3.036	3.629

Specimen Stability

To evaluate sample stability for all claimed parameters in predilute mode a total of 20 residual K2EDTA whole blood samples were prepared and stored at the defined condition for each specimen. Each sample was analyzed in duplicate at different time points according to the study design. The sample stability at room temperature for all parameters was established at 15 minutes from the time of sample preparation (dilution).

To evaluate sample stability of whole blood (undiluted) samples, 21 normal and 15 abnormal whole blood specimens were collected and analyzed on three to four DxH 520 instruments. Sample stability was performed at both room temperature and refrigerated storage. All parameters reported on DxH520 were assessed. 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 in the whole blood mode for RBC, HGB, MCV, HCT, MCH, MCHC, RDW, RDW-SD, PLT, and MPV is 24 hours at room temperature (18–26°C) and refrigerated temperature (2–8°C) while the sample stability for WBC and the 5-part differential parameters is 24 hours at room

temperature (18–26°C) and 8 hours at refrigerated temperature (2–8°C) from the time of collection.

Comparison Studies

Pre-Dilute vs. Whole Blood Sampling Modes

To demonstrate equivalency between pre-dilute and whole blood modes, fresh whole blood samples were collected within 8 hours of venipuncture in K₂EDTA collection tubes. Whole blood (normal and abnormal) samples run in duplicate in the Cap Pierce mode was compared to two K₂EDTA whole blood dilutions prepared by the operator run in the pre-dilute mode. Deming and weighted Deming approaches were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals and correlation coefficient) of the comparison. Results met the predefined acceptance criteria and were found to be acceptable.

Sampling Modes (Cap Pierce, Open Vial and Tube Holder Open Vial)

Cap piercing, open-vial and tube holder open-vial (THOV) modes were tested with the same blood samples on the same instrument using the same reagents. A total of 44 samples (normal and abnormal) were included in analysis for the mode equivalency testing. Deming and weighted Deming regressions were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals and correlation coefficient) of the comparison. Results met the predefined acceptance criteria and were determined to be acceptable.

Anticoagulant and Matrix Comparison

K₂EDTA and K₃EDTA anticoagulant and matrix (venous or capillary) comparison studies were conducted in the whole blood cap-piercing mode. K₂EDTA venous whole blood was compared to K₃EDTA venous whole blood or K₂EDTA capillary whole blood. A total of 49 samples (normal and abnormal) were included in the analysis for the anticoagulant comparison and a total of 48 samples were included in analysis for the matrix comparison. Deming and weighted Deming regressions were used to estimate the regression model (slope, intercept, 95% confidence intervals and correlation coefficient) for the comparisons. The results met the predefined acceptance criteria and were found to be acceptable.

Reference Intervals

The normal adult reference interval for all parameters reported by the DxH 520 system were established by analyzing whole blood samples collected in K₂EDTA from a total of 279 healthy individuals (N=126 males, N=153 females). Statistical analysis was performed using the nonparametric method in accordance with the reference limits calculated using 95% confidence intervals.

A literature reference interval verification study was performed for the pediatric population. A total of 208 samples were collected from apparently healthy pediatric patients in pediatric subcategories (0 to 30 days (n=20), 31 days to 2 years (n=27), 3 to 12

years (n=94) and 13 to 21 days (n=67)) to support the Intended Use. All samples were collected in K₂EDTA anticoagulant and analyzed in the whole blood sampling mode.

K. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable

L. Conclusion:

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