510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k120771

B. Purpose for Submission:

Updated system software (version 2.0)

C. Manufacturer and Instrument Name:

Beckman Coulter, Inc.; UniCel® DxH 800 COULTER® Cellular Analysis System

D. Type of Test or Tests Performed:

Quantitative test for 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, and body fluid (TNC and RBC) parameters

E. System Descriptions:

1. Device Description:

The UniCel® DxH 800 Coulter® Cellular Analysis System update with version 2.0 software has the same intended use and utilizes the same principles of operation, reagents, controls and calibrators as the original cleared device.

The DxH 800 system is comprised of the analyzer (Sample Processing Module - SPM) and a suite of analytical reagents that allow for simultaneous quantitative determination of hematological parameters through the use of impedance, radio frequency (RF), flow cytometric light scatter, spectrophotometry, and supravital staining methodologies. Additional reagents provide system cleaning, quality control and calibration.

2. Principles of Operation:

The Coulter Principle of automated cell counting and sizing is used in the analysis of the whole blood and body fluid specimens. Each cell suspended in a conductive liquid (diluent) acts as an insulator. As each cell goes through the aperture, it momentarily increases the resistance of the electrical path between two submerged electrodes on either side of the aperture. This causes a measurable electronic pulse. While the number of pulses indicates particle count, the amplitude of the electrical pulse is proportional to the cell volume. These pulses are sent to the Signal Conditioner for analog to digital conversion. Pulse counts and digitized pulse measurements are sent to the System

Manager for processing by the algorithms where the reported parameter values, flags and histograms are generated.

The lytic reagent used for the white cell count prepares the blood so the system can count leukocytes and measure the amount of hemoglobin. The lytic reagent rapidly and simultaneously destroys the erythrocytes and converts a substantial proportion of the hemoglobin to a stable pigment while it leaves leukocyte nuclei intact. The absorbance of the pigment is directly proportional to the hemoglobin concentration of the sample.

Hemoglobin is measured photometrically at 525 nm using the sample from the white cell analysis. Clean diluent is introduced into the cuvette during each operating cycle and is used as a blank in the calculation of the HGB.

The COULTER® VCSn technology is used to determine the white cell differential, nucleated red blood cell count and reticulocyte parameters along with associated flags, messages, histograms and data plots.

The sample preparation and analysis uses specific reagents and analytical processes for the WBC differential, NRBC and Retic analysis. The prepared sample is delivered to the flow cell for sample detection. As the cells pass through the sensing zone, a diode laser illuminates the particles causing light scatter and light absorption. Simultaneously to the light scatter measurements, cell volume and cell conductivity are also measured.

The data collected during each of the analytical processes is transferred to the System Manager where the digital raw values are processed by the algorithm using mathematical approaches designed for finding optimal separation between clusters of data. The identified clusters are used to calculate the frequency of cells within each population, generate parameter values, flags, histograms and data plots.

3. Modes of Operation:

   Automated Cassette Closed Vial (whole blood analysis mode)

   Manual Single Tube Closed Vial (whole blood analysis mode)

   Manual Single Tube Open Vial (1 in 5 pre-diluted whole blood mode; body fluid analysis mode)

4. Specimen Identification:

   Specimen identification is automated or by manual sample identification with the use of a hand held barcode scanner.

5. Specimen Sampling and Handling:

   The DxH 800 provides the user with the ability to obtain a variety of combinations of

parameter results through the use of analytical test panels. In addition, specimen analysis can occur via a number of sampling methods on the analyzer (see modes of operation above).

6. Calibration:

   COULTER® S-CAL® Calibrator (k862122) is used for determining calibration factors to ensure accurate measurements of directly measured CBC parameters. Assigned assay values are traceable to reference methods.

7. Quality Control:

   COULTER® 6C Cell Control (k081822) enables monitoring of system performance for all directly measured and calculated CBC, Diff and NRBC parameters.

   COULTER® Retic-X Cell Control (k930119) monitors system performance of the reticulocyte parameters.

   COULTER® LIN-X Linearity Control (k081641) verifies the reportable range, and assesses the calibration of the WBC, RBC, HGB, and PLT parameters.

   COULTER® Body Fluid Control (k082162) monitors system performance of the body fluid cycle's RBC and TNC count parameters. Additionally, COULTER Body Fluid Control can be used for verification of the measuring range and linearity of the TNC and RBC in the body fluid panel.

   COULTER® LATRON™ CP-X Control (k885028) determines calibration factors to ensure accurate measurements of directly measured CBC parameters. Assigned assay values are traceable to reference methods.

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 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)
    - 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, RDW-SD, PLT, MPV
- Body Fluids (cerebrospinal, serous and synovial)
    - TNC and RBC

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; k081930

2. Comparison with Predicate Device:

Similarities		
Item	Device: UniCel® DxH 800 Update (Software 2.0)	Predicate: UniCel® DxH 800
Intended Use and Function	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) – 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, RDW-SD, PLT, MPV • Body Fluids (cerebrospinal, serous and synovial) – TNC and RBC	The UniCel® DxH 800 Analyzer is a quantitative, automated hematology analyzer for in vitro diagnostic use in screening patient populations found in clinical laboratories. The UniCel® DxH 800 Analyzer provides a: • Complete Blood Count (CBC), Leukocyte 5 Part Differential (Diff), Reticulocyte (Retic) and Nucleated Red Blood Cell (NRBC) on whole blood • Total Nucleated Count (TNC) and Red Cell Count (RBC) on Body Fluids (cerebrospinal, serous and synovial) (BF)
Principles of Measurement: WBC, RBC, MCV, Plt, BF-TNC, BF-RBC	Aperture impedance (Coulter® Principle)	Same
Principle of Measurement: Hgb	Spectrophotometric	Same
Principles of Measurement: WBC Differential, Retic & NRBC	VCSn Technology using: • Aperture impedance (DC) • Conductivity (RF) • Laser Light Scatter (Multiple angles) • Laser Light Absorbance	Same
Analysis Reagents	COULTER® DxH Diluent COULTER® DxH Diff Pack COULTER® DxH Retic Pack COULTER® DxH Cell Lyse	Same
Quality Controls & Calibrator	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	Same
Cleaning Agent	COULTER® DxH Cleaner	Same
System configuration	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	Same

Similarities		
Item	Device: UniCel® DxH 800 Update (Software 2.0)	Predicate: UniCel® DxH 800
	Windows XP application specific software Handheld Barcode Scanner Printer	
Aspiration Pathway	Single sampling probe and common aspiration pathway used for all sample presentation modes	Same
Sample Aspiration Volume	Automatic, cap-piercing: 165 µL Single tube - open-vial and cap pierce: 165 µL Predilute 165 µL - fixed ratio of 1 in 5 dilution of blood with diluent	Same
Sample Preparation	Rotary blood sampling valve (BSV) and syringe aspiration / dispense for blood segmentation / distribution Rotary ceramic piston pumps driven by stepper motors for reagent delivery CBC dilutions mixed vial tangential delivery to baths VCSn dilutions mixed by air jet in reaction chambers Reagents are temperature stabilized for analysis reactions	Same
Throughput : Automated cassette processing	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 Throughput is based on normal specimens – analytical cycle times are increased with cytopenic specimens	Same

Differences		
Item	Device: UniCel® DxH 800 Update (Software 2.0)	Predicate: UniCel® DxH 800
Sampling Mechanism	Same as predicate with: • Updates to provide dedicated cassette and mixing profile for specific tubes	Single tube presentation – open and closed vial sampling Automated presentation – closed vial sampling from 5 position cassette Maximum initial load capacity 20 racks
Mechanisms for processing	Same as predicate with: • Updates for device reliability, manufacturability and serviceability	Mechanisms to achieve process of: automated cassette transportation and specimen

Differences		
Item	Device: UniCel® DxH 800 Update (Software 2.0)	Predicate: UniCel® DxH 800
		mixing (by rocking), sample aspiration, sample preparation, sample and reagent presentation to analytical modules, sample analysis, raw data collection, algorithmic processing and data reporting Cassette transportation by magnetic drive allowing multi-directional moves and capability to return cassette to sampling position for repeat / reflex testing
Sample identification	Same as predicate with: • Corrections to address sample identification related recalls • Updates to add capability for host query communication with Laboratory Information System (LIS)	Sample aspiration module (SAM) mounted barcode reader for automated barcode reading of cassette and sample tube identifiers Manual barcode scanning of sample tube identifier (Handheld scanner) Manual keyboard entry of sample identifier
Data Analysis	Same as predicate with: • Enhancements for improved flagging	Raw information is digitized from all analytical modules and passed to workstation for algorithmic processing Algorithms using advanced mathematical methods for population differentiation and flagging centralized within workstation
Data reporting	Same as predicate with: • Corrections to address data reporting related recalls • Updates to include revised LIS communication protocol to improve software performance and additional printer support functions	Workstation display graphics, hardcopy printing and transmission to Laboratory Information System (LIS)
Controlling software	Same as predicate with: • Corrections to address software related recalls • Updates to improve removal of cleaning agent during Shutdown and Daily Checks and monitoring of Sample and Sheath pressure sensors reading to detect when sensors are disconnected	System software (embedded and workstation) designed specific to support all features of DxH 800. The software system consists of a Data Manager component, a System Manager component (including algorithms), the User Interface, all of which are

Differences		
Item	Device: UniCel® DxH 800 Update (Software 2.0)	Predicate: UniCel® DxH 800
	• Software architecture changes that provide a foundation for future product enhancements and platform expansion	resident in the Workstation. In addition an Embedded Application is resident in the analyzer. The Embedded application uploads from the workstation on system power-up Extensive real time monitoring and reporting of system status including: • Component and module activities • System Voltages and Currents • System Pressure and Vacuum • System Temperatures • Motor activity • Mechanism Sensor status • Reagent Pump Operation • Raw data collection
Performance Claims	Performance claims are the same as the predicate DxH 800 with the following updates based on alignment to current clinical testing standards: • Updated Operating and Measuring ranges for selected parameters To align selected parameter lower limits with background, Limit of Blank, Limit of Detection and Limit of Quantitation To align selected upper parameter limits with values seen in clinical conditions • Updated NRBC Carryover specification	As stated in the Instructions for Use for the predicate device

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

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

CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition

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

CLSI EP6-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 H56-A, Body Fluid Analysis for Cellular Composition; Approved Guideline

CLSI EP9-A2, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition

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

CLSI C28-A3, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition

CLSI EP15-A2, User Verification of Performance for Precision and Trueness; Approved Guideline-Second Edition

CLSI H3-A6, Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard-Sixth Edition

CLSI H4-A6, Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard-Sixth Edition

J. Performance Characteristics*:*

1. Analytical Performance:

a. Accuracy:

Whole Blood (WB) Comparability

A total of 952 whole blood specimens were analyzed at four test sites. Each of the samples was analyzed in duplicate on the updated DxH 800 and on the predicate device to obtain a Complete Blood Count, WBC Differential, including NRBC's, and Reticulocyte measurements. For each whole blood sample, two manual wedge smears were prepared and stained using a Wright-Giemsa stain. A manual (reference) 200-cell differential was performed on each of the prepared stained blood films by different technologists to obtain a 400-cell differential according to CLSI H20-A2. For neonate and infant specimens, a single analysis was performed on the updated DxH 800 and the results from the test sites' clinical analyzer were used as the predicate device results. In addition, a single blood film and single 200-cell differential was performed.

The results from the first replicate for each of the specimens from the test and predicate devices and the results of the manual differential were used for the comparison analysis. All data passed specifications.

Body Fluid (BF) Comparability

A total of 289 body fluid specimens, collected across three sites, were analyzed by the test device and manual reference. Of these, 166 were also analyzed on the predicate device. Each of the samples was analyzed in duplicate on the updated DxH 800 and reference manual chamber counts were performed. If the volume of specimen permitted it was also analyzed in duplicate on the predicate device. The results from the first replicate for each of the specimens from the predicate and test devices and the results of the manual chamber count were used for the comparison analysis. All data passed specifications.

Clinical Sensitivity/Specificity

A total of 870 whole blood specimens were analyzed for the clinical sensitivity and specificity testing at four test sites. Each of the specimens was analyzed in duplicate on an updated DxH 800 and the predicate device. For each whole blood specimen, two wedge smears were prepared and stained using a Wright-Giemsa stain. A manual (reference) 200-cell differential was performed on each of the prepared stained blood films by different technologists to obtain a 400-cell differential according to CLSI H20-A2. For neonate and infant specimens, a single analysis was performed on the updated DxH 800 and the results from the test sites' clinical analyzer were used as the predicate device results. In addition a single blood film and single 200-cell differential was performed. The presence or absence of an abnormality on the blood film, i.e., reference positive or negative was determined using The International Consensus Group for Hematology Review guideline: Suggested Criteria for Action Following Automated CBC and WBC Differential Analysis.

The DxH 800 Suspect messages from the first specimen replicate were compared to the reference manual differential to determine the true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN). The clinical sensitivity and specificity was calculated from the combined data from all sites, for each of the Suspect messages (Blasts, Variant Lymphocyte, Left Shift or Immature Granulocyte) generated by the updated DxH 800. In addition, an "Overall" analysis assessment was performed where the presence of any one suspect message was considered to represent detection of an abnormal sample for the updated DxH 800 and the predicate. Analysis of the data collected demonstrates that the updated DxH 800 provided equivalent performance for Clinical Sensitivity and Specificity of the differential suspect messages as compared to the predicate device analyzing the same data set.

Clinical Sensitivity and Specificity:

All Sites Combined "Overall" and by individual suspect message

	Overall	Blasts	Variant Lymphs	Left Shift	Immature Granulocytes
TP	143	39	37	41	75
TN	581	758	767	714	724
FP	116	50	45	109	62
FN	30	23	21	6	9
Total	870	870	870	870	870
% Sensitivity (TP)	82.66	62.90	63.79	87.23	89.29
95% Lower Limit (TP)	77.02	50.88	51.42	77.69	82.67
95% Upper Limit (TP)	88.30	74.93	76.16	96.77	95.90
% Specificity (TN)	83.36	93.81	94.46	86.76	92.11
95% Lower Limit (TN)	80.59	92.15	92.88	84.44	90.23
95% Upper Limit (TN)	86.12	95.47	96.03	89.07	94.00
% Efficiency	83.22	91.61	92.41	86.78	91.84

Clinical Sensitivity and Specificity:

Test vs. Predicate - Overall flagging

	Overall	Blasts
TP	143	123
TN	581	582
FP	116	117
FN	30	51
Total	870	873
% Sensitivity (TP)	82.66	70.69
95% Lower Limit (TP)	77.02	63.93
95% Upper Limit (TP)	88.30	77.45
% Specificity (TN)	83.36	83.26
95% Lower Limit (TN)	80.59	80.49
95% Upper Limit (TN)	86.12	86.03
% Efficiency	83.22	80.76

b. Precision/Reproducibility:

Imprecision (Reproducibility)

Reproducibility testing was performed on the updated DxH 800 to demonstrate the long term imprecision of the device using multiple levels of control materials (3 levels of 6C Cell Controls and 3 levels of Body Fluid Controls) for CBC, Differential, NRBC, Reticulocyte and Body Fluid parameters. Testing was conducted at four test sites using a single lot of each product throughout the test period. At three of the test sites; each level of control was analyzed in duplicate, twice a day, for a minimum of 20 days and 14 days of data was collected at site 4. Data from site 4 was accepted and included in the analysis.

Data were analyzed separately for each site and for the pooled data from all sites

using all replicates. For each site, the coefficient of variation (CV) and standard deviation (SD) for between-day, within-day, within-run, and within-lab were estimated. For pooled data on the STA-R® analyzer from the three sites, the CV and SD for between-site, between-day, within-day, within-run, within-lab and reproducibility were estimated. All data passed defined acceptance limits.

Imprecision (Repeatability)

Repeatability testing was performed on the updated DxH 800 to demonstrate the short term imprecision of the device. Testing was performed at four sites using replicate measurements of specimens in the normal range, at medical decision levels and over the analytical measuring interval using whole blood (or control products at specified target ranges), pre-diluted whole blood and body fluid specimens. An n=10 replicates was targeted for each specimen. At least three specimens were analyzed in each of the defined target ranges. Each specimen within a parameter target range was tested in a different analytical cycle (CBC (C), CBC/DIFF (CD), CBC/DIFF/Retic (CDR), CBC/Retic (CR), and Retic (R)). All data for each specimen analyzed at all test sites was pooled and modeled as a precision profile. The precision profile was then used to estimate imprecision at defined levels over the analytical measuring interval.

The mean, SD and %CV were calculated for each specimen. These data were combined to build precision profiles. This approach is based on the %CV of repeated measurements from all samples modeled as a function of their means in accordance with CLSI EP05-A2 and H26-A2 standards. Profiles were calculated using all samples, combining the analytical modes and instruments at all sites. All data passed defined acceptance limits.

Pre-Dilute Imprecision (Repeatability)

Ten whole blood specimens were selected to provide a broad coverage of the measuring ranges for the parameters for which repeatability claims are made (WBC, RBC, HGB and PLT). Testing was conducted at two test sites. For each whole blood sample selected, 10 separate 1:5 dilutions were prepared. Each prepared dilution was analyzed using the pre-dilute analytical cycle of the updated DxH 800. The pre-dilute analytical cycle only provides results for CBC parameters.

The same analytical approach of using precision profiles, as described in the whole blood repeatability imprecision analysis, was used for the pre-dilute analysis. All data passed defined acceptance limits.

Body Fluid Imprecision (Repeatability)

Body Fluid specimens were selected based on parameter values within specific test ranges. Three test sites ran at least three samples at each defined test range using any of the body fluid types (cerebrospinal, serous or synovial). Twenty seven (27) and 34 body fluid specimens were used for the BF-RBC and BF-TNC measurands

respectively. The same analytical approach of using precision profiles, as described in the whole blood imprecision analysis, was used for the body fluid analysis. All data passed defined acceptance limits.

c. Linearity:

Linearity testing by serial dilution was conducted at one test site. Linearity was assessed by performing multiple measurements on specimens diluted to cover the analytical measuring interval (AMI). The concentrations were prepared so that the relative concentration of each sample was known. Linearity analysis for WBC and PLT parameters was performed in three separate dilution series, indicated as "Low", "Mid" and "High". The RBC, HGB, BF-TNC and BF-RBC parameters were assessed with two separate dilution series indicated as "Mid" and "High". For each of the high target value specimens, a series of 10 dilutions were prepared. The dilutions were prepared using DxH Diluent as the Low (LTV). Each dilution within the dilution series was analyzed in triplicate in random order using the CBC/Differential (CD) analytical cycle on the updated DxH 800. All data passed specifications.

d. Carryover:

Testing was performed to demonstrate whole blood and body fluid carryover performance of the updated DxH 800. Whole blood carryover was assessed by running whole blood specimens with high parameter values followed by diluent samples. This testing was performed to assess carryover within and between the different analytical cycles (test panels) on the updated DxH 800. Testing was conducted at four sites to cover all combinations of analytical cycles (i.e., C, CD, CDR, CR, R). The testing was performed by running the selected high whole blood specimen three times followed by the analysis of three diluent specimens (a new diluent specimen was used for each analysis). For whole blood, the WBC, RBC, HGB & PLT parameters, carryover is calculated as:

%Carryover = [(diluent 1 - diluent 3) / (blood sample 3 - diluent 3)] x100

For the NRBC, Differential and Retic analysis carryover is reported as total events (cells) counted in each of the diluent specimens. All data passed acceptance limits.

Measurand	% Carryover
WBC	≤ 0.50%
RBC	≤ 0.50%
HGB	≤ 1.00%
PLT	≤ 1.00%
Measurand	Carryover (events or cells counted)
NRBC	≤ 75 events (WBC = 0 - 300 x 10^3/µL) ≤ 100 events (WBC > 300 x 10^3/µL)
DIFF	≤ 200 events
Retic	≤ 600 events

Body Fluid Carryover

Carryover that could influence a body fluid result was assessed by running whole blood specimens with high parameter values followed by diluent analyzed in the body fluid analytical cycle. Testing was conducted at four sites to assess all analytical cycles (i.e., C, CD, CDR, R) preceding a BF analytical cycle. The carryover testing was performed by running the selected high whole blood specimen three times followed by the analysis of three diluent specimens in the BF analytical cycle (a new diluent specimen was used for each analysis). For Body Fluid parameters, carryover is calculated as the cell counts in each of the diluent specimens from the analysis. All data passed specifications.

Measurand	Carryover (events or cells counted)
BF-RBC	≤ 1000 events
BF-TNC	≤ 20 events

e. Interfering Substances:

Refer to the DxH 800 predicate device (k081930).

2. Other Supportive Instrument Performance Data Not Covered Above:

a. Stability Studies:

Testing was performed on the updated DxH 800 to demonstrate whole blood specimen stability. Testing was performed on whole blood specimens at various time intervals (long-term and short-term) and stored at refrigerated and room temperature. In addition, testing was performed on pre-diluted specimens.

Long Term Stability

Forty-one normal specimens were collected for the room temperature long-term stability study, and 41 normal specimens were collected for the refrigerated long-term stability. Twenty-one of the specimens were common to both studies. Testing was conducted at three test sites. For each of the specimens selected, sufficient aliquots were prepared to allow analysis of a new aliquot at each of the defined time intervals and storage temperatures.

Time zero (T0) results were established by analyzing each blood specimen within two hours of collection. At the storage time intervals, a new specimen aliquot was removed from storage, and prior to analysis, aliquots were manually mixed by inversion 20 times. In addition, those removed from refrigerated storage were allowed to equilibrate to room temperature for 30 minutes and then hand mixed again by inversion 20 times prior to placing on the device for analysis. Each aliquot was analyzed in duplicate to obtain CBC, Differential and Retic results.

The upper limit of the drift was compared to the specification. The data was

considered to meet specification when the 95% upper limit of drift for a parameter was less than the specification limit for the parameter. All data passed specifications.

Short Term Stability

Specimens were collected from 11 volunteers from the Beckman Coulter donor program. Blood from each volunteer was drawn into both K_2 and K_3 EDTA tubes for a total of 22 specimens. For each of the specimens, sufficient aliquots were prepared to allow a new aliquot to be analyzed at each of the defined time intervals. Time zero results were established by analyzing each blood specimen in duplicate within five minutes of collection. At the storage time intervals, a new specimen aliquot was removed from storage. This testing was only performed on specimens stored at room temperature as the short storage durations make refrigerated storage impractical. After removal from storage, each specimen was manually mixed by inversion 20 times prior to being placed on the device for analysis in duplicate to obtain CBC, Differential and Retic results.

The claims were met when the 95% upper limits of the drift for a parameter was less than the specification for the parameter. All data passed specifications.

Pre-dilute Stability

Testing of 37 clinical whole blood samples was performed at two test sites. For each specimen selected, a primary 1:5 dilution was prepared. Sufficient aliquots were prepared to allow analysis of a new pre-dilute aliquot at each of the defined time intervals. Time zero (T0) results were established by analysis of the dilution immediately after preparation. At the storage time intervals, a new pre-diluted specimen aliquot was removed from storage and each pre-diluted aliquot was manually mixed and analyzed in duplicate using the pre-dilute test panel on the device to obtain CBC results.

The claims were met when the 95% upper limits of the drift for a parameter was less than the respective acceptance limit for the parameter. All data passed specifications.

b. Accuracy (Comparability) - Analytical Cycles

Testing was performed on the updated DxH 800 to demonstrate equivalency of results (within defined limits) between the whole blood analytical cycles (test panels), CBC (C), CBC/DIFF (CD), CBC/DIFF/Retic (CDR), CBC/Retic (CR), Retic (R) when specimens are analyzed using the automated closed vial sampling method. In addition, testing was performed to demonstrate equivalency between specimens analyzed as whole blood and as Pre-dilute (PD) specimens.

Whole Blood – Analytical Cycle Comparability

Testing was performed on the updated DxH 800 to demonstrate equivalency of results

(within defined limits) between the whole blood analytical cycles (test panels), CBC (C), CBC/DIFF (CD), CBC/DIFF/Retic (CDR), CBC/Retic (CR), Retic (R) when specimens are analyzed using the automated closed vial sampling method. A total of 50 whole blood specimens were analyzed in the study. Testing was conducted at a single test site. All specimens were analyzed in duplicate in each of the analytical cycles (test panels) using the automated closed vial sampling method. All data passed specifications.

Whole blood vs. Pre-dilute Analytical Cycle Comparability

Testing was performed on the updated DxH 800 to demonstrate equivalency of results (within defined limits) between specimens analyzed as whole blood and pre-diluted blood. A total of 58 clinical specimens were collected for the study. Testing was conducted at two test sites. All specimens were analyzed in duplicate as a whole blood specimen and as a 1:5 dilution. The whole blood specimens were analyzed using the CBC, Differential and Retic (CDR) analytical cycle using the automated closed vial sampling method and the prepared pre-diluted specimen was analyzed using pre-dilute analytical cycle using the manual single tube closed vial sampling method. All data passed specifications.

c. Accuracy (Comparability) - Sampling Methods

Testing was performed to demonstrate comparability between the sampling modes available on the updated DxH 800. Testing compared: 1) the automated closed vial with the manual closed-vial sampling, and 2) the manual closed-vial with the manual open vial methods using the CBC, Differential and Retic analytical cycle.

Automated closed-vial vs. Manual closed-vial Comparability
A total of 45 whole blood specimens were analyzed in the study at a single test site. All specimens were analyzed in duplicate using automated closed-vial and manual closed-vial sampling methods using the CBC, Differential and Retic (CDR) analytical cycle. All data passed specifications.

Manual closed-vial vs. Manual open-vial Comparability
A total of 44 whole blood specimens were analyzed in the study at a single test site. All specimens were analyzed in duplicate using manual closed-vial and manual open-vial sampling methods using the CDR panel. All data passed defined specifications.

d. Anticoagulant types

Testing was performed on the updated DxH 800 to demonstrate equivalency of results for whole blood specimens collected into K_2 and K_3EDTA anticoagulant. Two venous specimens were collected prospectively by venipuncture from each donor: one into a tube containing K_2EDTA, the other containing K_3EDTA. Specimens were collected from 127 volunteers from the Beckman Coulter donor program. All specimens were analyzed in duplicate on a single test device to obtain CBC,

Differential and Retic results using the instrument automated closed vial sampling method. All data passed specifications.

e. Collection Method

Testing was performed on the updated DxH 800 to demonstrate equivalency of results for specimens collected by venipuncture and capillary collection methods. Two venous tubes were collected prospectively from each donor, one by venipuncture, the other by finger stick (capillary) into tubes containing a salt of EDTA. Specimens were collected from 53 volunteers from the Beckman Coulter donor program. All specimens were analyzed in duplicate to obtain CBC, Differential and Retic results using the instrument sampling method applicable to the specimen type (automated closed-vial for the venous specimen and the manual open-vial for the capillary specimen). All data passed specifications.

f. Determination of limit of blank, lower limits of detection and quantitation:

Limit of Blank (LoB):

DxH Diluent samples were used as the blank specimen for the LoB testing since within the analytical process the diluent is the primary contributor to any impact to the blank results. Each blank specimen tube was sampled only once. Whole blood specimens were manipulated to obtain the cellularity required. Cells from whole blood were used to generate specimens of appropriate cellularity for the testing as Body Fluid specimens having appropriate cellularity and volume are not readily available. Testing was conducted on three updated DxH 800 systems at the Beckman Coulter Clinical Quality Assurance laboratory.

Whole Blood: A total of 160 diluent specimens (blank) were analyzed. Thirty-two tubes of diluent were analyzed each day for five days. Sixteen tubes were analyzed in the morning and 16 in the afternoon. The tubes were divided into four groups of four tubes. Each group was analyzed in one of the four DxH 800 test panels that analyze and report whole blood WBC and PLT counts (CBC, CBC/DIFF, CBC/DIFF/Retic, and CBC/Retic).

Body fluid: A total of 150 diluent specimens (blank) were analyzed. Thirty tubes of diluent were analyzed each day for five days. Fifteen tubes were analyzed in the morning and 15 tubes in the afternoon using the Body Fluid test panel. Results for the LoB met specifications.

Limit of Detection (LoD)

To determine the LLoD, the standard deviation of sample measurements is obtained from repeated measurements of samples with relevant low concentrations. A concentration in the range from the LoB to approximately 4x LoB was used to obtain data to be used to estimate precision at these levels. Primary specimens for each of

the parameters to be tested were prepared to achieve cell concentration of approximately 4x the LoB specification.

Four different whole blood specimens were used to generate four different primary specimens, one for each of the parameters to be analyzed, for a total of 16 primary specimens. Using these primary specimens as the 100% concentration, a series of 10 dilutions were prepared, using DxH Diluent as the blank to dilute the specimen. Each of the series of concentrations was analyzed n = 5 on each of the test devices on the day they were prepared (Day 1) and n = 5 on the following day (Day 2) for a total of ten replicates per level. Results for the LLoD met specifications.

Limit of Quantitation (LoQ)

The lower limit of quantitation (LLoQ) was calculated based on experimental data collected during the estimation of the LLoD to estimate within laboratory precision and bias. Analytical bias (difference from reference) of the test devices was established by duplicate analysis of five specimens having values established from a reference device whose calibration is traceable to whole blood reference methods. This process was performed on each of the eight days over which the LLoD testing occurred and was used in the LLoQ calculations as "Bias".

Using the defined device accuracy and precision specification, expected Total Error (TE) was determined for the LLoD specification level. The LLoQ data are considered to be acceptable if the TE estimated from the testing is less than the expected TE calculated from the LLoQ acceptance limits defined in the requirements. Results for LLoQ passed acceptance limits.

g. Reference Intervals:

Confirmatory testing was performed on the updated DxH 800 to demonstrate comparability of whole blood reference ranges for an adult population to the ranges established for the predicate device. Prospective samples were collected in K_2EDTA from a total of 127 volunteers (male=61; female=66) from the Beckman Coulter donor program. All specimens were analyzed in duplicate on a single test device to obtain CBC, Differential and Retic results using the closed vial sampling method.

The upper and lower parameter value limits of the established reference range, as provided in the predicate device labeling were compared to the current, confirmatory data set using a non-parametric approach. Limits were considered to not differ statistically when the 95% confidence intervals of the upper and lower limits of the two data sets overlapped. The reference ranges established for the predicate DxH 800 are applicable for the updated DxH 800. The updated DxH 800 labeling will provide the reference ranges as currently presented in the predicate labeling.

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.