April 23, 2019

Beckman Coulter
Samy Puccio
Staff Regulatory Affair Specialist
11800 SW 147th Ave
Miami, Florida 33196-2500

Re: K181475
Trade/Device Name: DxH 520 Hematology Instrument
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated differential cell counter
Regulatory Class: Class II
Product Code: GKZ
Dated: June 1, 2018
Received: June 4, 2018

Dear Samy Puccio:

This letter corrects our substantially equivalent letter of March 1, 2019.

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 and the limitations described below. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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.

The Office of In Vitro Diagnostics and Radiological Health has determined that there is a reasonable likelihood that this device will be used for an intended use not identified in the proposed labeling and that such use could cause harm. Therefore, in accordance with Section 513(i)(1)(E) of the Act, the following limitation must appear in the **Intended Use** statement of the device's labeling:

*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.*

Furthermore, the intended use/indication 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.*

must be prominently displayed in all labeling, including pouch box, and carton labels, instructions for use, and other promotional materials, in close proximity to the trade name, of a similar point size, and in bold print.

Please note that the above labeling limitations are required by Section 513(i)(1)(E) of the Act. Therefore, a new 510(k) is required before these limitations are modified in any way or removed from the device's labeling.

The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market. This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification if the limitation statement described above is added to your labeling.

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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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 comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Timothy T. Stenzel -S

Timothy Stenzel, MD, PhD
Director
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K181475

Device Name
DxH 520 Hematology Instrument

Indications for Use *(Describe)*
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.

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)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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| Section 5 | 510(k) Summary |
|---|---|

# 510(k) Summary for
# DxH 520 Hematology Instrument

**510(k) Owner / Submitter Information**
Name: Beckman Coulter Inc.
Address: 11800 SW 147th Ave., Miami, FL 33196
Phone #: (305) 380-4509
Fax #: (786) 639-2584
Contact Person: Samy Puccio
Email Address: spuccio@beckman.com

**Date Submitted**: June 1, 2018

**Device Name and Classification**
Trade Name: DxH 520 Hematology Instrument
Common Name: DxH 520
Classification: Class II
Classification Name: Automated differential cell counter (21 CFR 864.5220)
Product Code: GKZ
Panel: Hematology

Predicate Device Information

| Predicate Product | 510(k) Number | Date Cleared | Classification | 21 CFR | Product Code |
|---|---|---|---|---|---|
| UniCel® DxH 800 Coulter® Cellular Analysis System | K140911 | 09/05/2014 | Class II | 864.5220 | GKZ |
| Manually prepared blood films per the manual wedge-pull film technique as described in CLSI H20-A2, Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrument Methods; Approved Standard – Second Edition | N/A | N/A | N/A | N/A | N/A |

## Device Description

The DxH 520 instrument provides a complete blood count (CBC with Five Part Differential (5PD)). Blood specimens are processed using a Closed Vial sampling method as default and have the option to run as Open Vial per operator selection.

RBC, WBC and PLT cell counts and sizes are determined using the Coulter Principle (impedance). The WBC 5 part differential is determined using a combination of the impedance WBC data and the direct optical measurement (Axial Light Loss - ALL) using a blue LED focused through the WBC aperture. With the addition of the DxH 500 Series Lyse, the RBCs are lysed and the released hemoglobin is converted into stable Oxyhemoglobin (or Carboxyhemoglobin, if present). The resulting complex is then measured by spectrophotometry.

The data obtained from the counting, sizing, optical and hemoglobin measurements is processed to create the DxH 520 hematological measurement that the device reports. Raw information is digitized from all analytical modules and passed to an embedded computer processing. Algorithms using dynamic gates to differentiate WBC subpopulations and flagging are performed within the embedded computer.

Controls and calibrators are used to monitor the performance of the instrument.

The compact bench top design of the DxH 520 will benefit small laboratories where bench space is limited. The integrated color display with graphical icon based user interface is intended to facilitate ease of use and operator training. The small bench-top DxH 520 instrument utilizes fully featured integrated software usually found on larger instrumentation.

## 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, 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.

**Technological Characteristics Comparisons to Predicate**

The tables below describe the similarities and differences between the predicate device, the DxH 800 Cellular Analysis System, and the DxH 520 Hematology Instrument.

**Table 1 - Intended Use and Function Similarities**

| Characteristic | UniCel DxH800<br>Predicate | DxH 520 | Similarity / Difference |
|---|---|---|---|
| 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.<br>The UniCel® DxH 800 Analyzer identifies and enumerates the parameters indicated below on the following sample types:<br>• Whole Blood (Venous and Capillary)<br>o 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<br>• Pre-Diluted Whole Blood (Venous and Capillary)<br>o WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV<br>• Body Fluids (cerebrospinal, serous and synovial)<br>o TNC and RBC | The DxH 520 is a quantitative, multi-parameter, automated hematology analyzer for in vitro diagnostic use in clinical laboratories; including hospital, reference, 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.<br>The DxH 520 Analyzer identifies and enumerates the measurands listed below on the following sample types:<br>• Whole Blood (Venous and Capillary)<br>o WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, NE%, NE#, LY%, LY#, MO%, MO#, EO%, EO#, BA%, BA#<br>• Pre-Diluted Whole Blood (Venous and Capillary)<br>o WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, NE%, NE#, LY%, LY#, MO%, MO#, EO%, EO#, BA%, BA#<br><br>The instrument is for use in adult and pediatric populations, including neonates.<br><br>LIMITATIONS<br>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. | The indications for use statements are the same for the CBC and 5 part differential Analysis measurands.<br><br>By design, the DxH 520 does not enumerate Reticulocytes or NRBC on whole blood, nor perform analysis of Body Fluid specimens.<br><br>By design, the DxH 520 enumerates WBC differential measurands on predilute sample types while the predicate does not. |

**Table 2 - Principles of Measurement Similarities**

| Characteristic | UniCel DxH800 Predicate | DxH 520 | Similarity / Difference |
|---|---|---|---|
| Principles of Measurement | | | |
| WBC, RBC, MCV, Platelet | Aperture impedance (Coulter® Principle) | Aperture impedance (Coulter® Principle) | Same as predicate |
| Hemoglobin | Spectrophotometric | Spectrophotometric | Same as predicate |
| WBC Differential | VCSn Technology using :<br>• Aperture impedance (DC)<br>• Conductivity (RF)<br>• Laser Light Scatter (Multiple<br>• angles)<br>• Laser Light Absorbance | Optical / Impedance<br>• Aperture impedance (DC)<br>• Light Absorbance (LED) –Axial Light Lost | The measurement methods of the DxH 520 are similar to the predicate.<br>The DxH 520 only uses impedance and Light absorbance in the WBC Differential measure. The light source for the optical method is an LED<br>The light source for DxH 800 optical is a Laser |
| Reticulocytes | VCSn Technology using :<br>• Aperture impedance (DC)<br>• Conductivity (RF)<br>• Laser Light Scatter (Multiple<br>• angles)<br>• Laser Light Absorbance | N/A | DxH 520 does not enumerate Reticulocytes |
| NRBC | VCSn Technology using :<br>• Aperture impedance (DC)<br>• Conductivity (RF)<br>• Laser Light Scatter (Multiple<br>• angles)<br>• Laser Light Absorbance | N/A | DxH 520 does not enumerate Reticulocytes |

**Table 3 - Reagents Similarities**

| Characteristic | UniCel DxH800 Predicate | DxH 520 | Similarity / Difference |
|---|---|---|---|
| Reagents | | | |
| Analysis Reagents | COULTER® DxH Diluent<br>COULTER® DxH Diff Pack<br>COULTER® DxH Cell Lyse<br>COULTER® DxH Retic Pack<br>COULTER® DxH Cleaner | DxH 500 Series Diluent<br>DxH 500 Series Lyse<br>DxH 500 Series Cleaner | Coulter DxH Diluent and DxH 500 Series Diluent have different formulation.<br>DxH 500 Series Lyse performs the functions of DxH Diff Pack and DxH Cell Lyse, i.e. lyse RBC's, convert HGB to stable pigment and maintain WBC's for counting and differential analysis.<br>COULTER® DxH Cleaner and DxH 500 Series Cleaner have the same formulation<br>DxH Retic- N/A since DxH 520 does not enumerate reticulocytes |
| Quality Controls & Calibrator | COULTER 6C Cell Control<br>COULTER Latron™ CP-X Control<br>COULTER RETIC-X Cell Control<br>COULTER LIN-X Control<br>COULTER Body Fluids Control<br>COULTER S-CAL® Calibrator kit | DxH 500 Series Control<br>DxH 500 Series Calibrator<br>DxH 500 Linearity Kit | The control and calibrator products both use human and animal cells to simulate human cell populations; each product is optimized for the reagents and technology used.<br>Linearity products both use human and animal cells to simulate human cell populations.<br>DxH 520 does not require products equivalent to the Latron, Retic and Body Fluids controls.<br>DxH 520 cell control, calibrator and linearity kit will have the same intended use as the DxH products. |

**Table 4 - Pre-Analytical Features Similarities**

| Characteristic | UniCel DxH800<br>Predicate | DxH 520 | Similarity / Difference |
|---|---|---|---|
| Pre-Analytic Features | | | |
| 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<br>PC based workstation running Microsoft Windows XP application specific software<br>Handheld Barcode Scanner<br>Printer | Bench top only<br>Integrated single board computer with color touch screen running application specific software using Linux OS<br>Handheld Barcode Scanner<br>Printer | Similar to predicate for the system configuration of benchtop, barcode scanner and printer<br><br>Different operating systems |
| Sampling Mechanism | Single tube presentation – open and closed vial sampling.<br>Automated presentation – closed vial sampling from 5 position cassette; Maximum initial load capacity 20 racks | Single tube manual open and closed vial | DxH 520 does not provide Automated presentation |
| Mechanisms for processing | Mechanisms to achieve process of :<br>Automated cassette transportation and specimen mixing (by rocking), sample aspiration, sample preparation, sample and reagent presentation to analytical modules, sample analysis, raw data collection, algorithmic processing and data reporting.<br>Cassette transportation by magnetic drive allowing multi-directional moves and capability to return cassette to<br>Sampling position for repeat / reflex testing. | Manual specimen mixing and presentation to the analyzer, user initiated sample aspiration followed by automatic sample preparation through sample and reagent delivery<br>to the analytical modules, followed by data collection, algorithmic processing and data reporting | DxH 520 provides manual open and closed vial<br>mechanisms for processing while predicate provides additional automated and closed vial sampling |
| Sample identification | 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 | Manual barcode scanning of sample tube identifier (Handheld scanner) Manual keyboard entry of sample<br>identifier | Automated: DxH 520 does not have automated sample identification mechanisms Manual sample identification same as predicate |

**Table 5 - Sample Processing Similarities**

| Characteristic | UniCel DxH800 Predicate | DxH 520 | Similarity / Difference |
|---|---|---|---|
| Sample Processing | | | |
| Aspiration Pathway | Single sampling probe and common aspiration pathway used for all sample presentation modes. | Single sampling probe for open and closed vial processing and single aspiration pathway. | DxH 520 has open and closed sampling mode with single aspiration pathway. |
| Sample aspiration volume | Automatic, cap-piercing : 165 µL<br>Single tube - open-vial and cap pierce:165 µL<br>Pre-dilute 165 µL - fixed ratio of 1 in 5 dilution of blood with diluent | Single tube - open and closed vial 16.7 µL<br><br>Pre-dilute 20µL whole blood + 300 µL diluent | DxH 520 aspirates the same volume for open and closed vial |
| Throughput | Automated cassette processing-<br>CBC ≥100 specimens per hour<br>CBC/Diff ≥100 specimens per hour<br>CBC/Diff/NRBC ≥ 90 specimens per hour<br>Any cycle with Retic ≥45 specimens per hour<br>(Throughput is based on normal specimens – analytical cycle times are increased with cytopenic specimens) | 55 Samples per hour in CP mode<br>60 Samples per hour in OV mode | Different throughput and processing types and rates for the DxH 520 and predicate |
| Data reporting | Workstation display graphics, hardcopy printing and transmission to Laboratory Information System (LIS) | Display of graphics, hardcopy printing and transmission to<br>Laboratory Information System (LIS) | Same as predicate |

**Table 6 - System Control Similarities**

| Characteristic | UniCel DxH800<br>Predicate | DxH 520 | Similarity / Difference |
|---|---|---|---|
| System Control | | | |
| Controlling software | System software (embedded and workstation) designed specific to<br>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 resident in the Workstation.<br>In addition an Embedded Application is resident in the analyzer. The Embedded application uploads from the<br>workstation on system power-up.Extensive real time monitoring and reporting of system status including:<br>Component and module activities,<br>• System Voltages and Currents<br>• System Pressure and Vacuum<br>• System Temperatures<br>• Motor activity<br>• Mechanism Sensor status<br>• Reagent Pump Operation<br>• Raw data collectionSingle sampling probe and common aspiration pathway used for all sample presentation modes. | System software designed specific to support all features of DxH 520 and DxH 500.<br>The Software runs on an integrated single board computer with color touch screen using Linux OS. Software provides all functions required for the User Interface, Data analysis, Results management, Instrument control and monitoring | DxH 520 software is designed with architecture to provide similar functions and capability as the DxH 800 within the DxH 520 design and architecture. |

**Table 7 – Performance Summary**

| STUDY | TESTING APPROACH | FDA GUIDANCE DOCUMENTS | STANDARDS/REFERENCES | TESTING RESULTS |
|---|---|---|---|---|
| Measurement Procedure Comparison | To compare the results (CBC and differential values) from test instruments versus the predicate DxH800 at clinical sites and small laboratory / physician office laboratory sites.<br><br>Comparison to manual microscopy as the reference method was performed for the WBC differential on the DxH 520 | Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells - Accuracy (Section 8) | CLSI H26-A2 Validation Verification and Quality Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210<br><br>CLSI H20-A2 Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved standard - Second Edition January 2007. FDA Standards Recognition #7-165<br><br>CLSI GP41-A6 Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard-Sixth Edition. October 2007. FDA Standards Recognition # 7-201<br><br>CLSI GP42-A6 Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard-Sixth Edition. September 2008. FDA Standards Recognition # 7-203 | The results support the accuracy claims for all parameters. The data presented shows substantial equivalency of the CBC and DIFF parameters to the DxH 800 predicate system at large clinical laboratories that include cancer centers, and at small laboratories with less experienced operators.<br><br>The DxH 520 is substantially equivalent to the reference method (manual slides) for the differential proportional parameters. |
| Precision | To assess precision of the DxH 520, three (3) studies were conducted: | Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells - Precision | CLSI H26-A2 Validation Verification and Quality Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210 | The long term precision (repeatability and reproducibility) meets the requirements as specified for all parameters |

| STUDY | TESTING APPROACH | FDA GUIDANCE DOCUMENTS | STANDARDS/REFERENCES | TESTING RESULTS |
|---|---|---|---|---|
| | Long Term Precision – Clinical and Small Laboratory/POL Sites,<br><br>Short term precision – Whole blood Repeatability,<br><br>Short term precision – Pre-Dilute Repeatability. | (Section 9) | CLSI EP05-A3 Evaluation of Precision Quantitative Measurement Procedures-Third Edition. September 2014. FDA Standards Recognition # 7-251<br><br>CLSI H20-A2 Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved standard - Second Edition January 2007. FDA Standards Recognition #7-165 | All whole blood repeatability acceptance criteria for all parameters were met.<br><br>All pre-dilute repeatability parameters met all requirements. The pre-dilute precision is highly dependent on the operator's preparation of the dilutions. |
| Precision | To assess operator to operator variability testing in both whole blood and pre-dilute modes at physician office laboratories or small laboratories with multiple operators. | Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells - Precision (Section 9) | No applicable standards. | The Operator to Operator Variability of pre-dilute and whole blood for between operator and within specimen are provided as performance characteristics only. The variability at small laboratories does not invalidate the results put forth by the instrument as the same users participated in the accuracy study where all specifications were met. The pre-analytical handling of samples in a POL setting provides accurate analysis on the DxH 520 and has low impact on operator variability. |
| Clinical Sensitivity | To assess the clinical sensitivity and specificity of the overall | Special Controls Guidance Document: Premarket | CLSI H26-A2 Validation Verification and Quality | The false negative samples were reviewed by the |

| STUDY | TESTING APPROACH | FDA GUIDANCE DOCUMENTS | STANDARDS/REFERENCES | TESTING RESULTS |
|---|---|---|---|---|
| | flagging on the DxH 520 as compared to the accepted reference method for differential determination, (manual slide counts). | Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells - Performance (Section 10) | Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210<br><br>CLSI H20-A2 Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved standard - Second Edition January 2007. FDA Standards Recognition #7-165<br><br>CLSI EP12-A2 User Protocol for Evaluation of Qualitative Test Performance, Approved Guideline – 2nd Edition. FDA Standards Recognition # 7-152<br><br>CLSI GP41-A6 Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard-Sixth Edition. October 2007. FDA Standards Recognition # 7-201<br><br>CLSI GP42-A6 Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard-Sixth Edition. September 2008. FDA Standards Recognition # 7-203 | Beckman Coulter Medical Director for their potential clinical impact. There were no FN's generated by blasts in this data set. Based on the Medical Director assessment none of the false negatives that occurred would have compromised patient diagnosis and treatment. The overall rate of FN was 13.5% with a sensitivity of 86.5% and specificity of 68.7%. |
| Linearity | Demonstrating that the reported results are directly proportional to the concentration of the | Special Controls Guidance Document: Premarket Notifications for | CLSI H26-A2 Validation Verification and Quality Assurance of Automated | The WBC, RBC Hgb and Plt parameters met the linearity specifications. |

| STUDY | TESTING APPROACH | FDA GUIDANCE DOCUMENTS | STANDARDS/REFERENCES | TESTING RESULTS |
|---|---|---|---|---|
| | measurand in a test sample for WBC, RBC, HGB, and PLT. | Automated Differential Cell Counters for Immature or Abnormal Blood Cells - Linearity (Section 11) | Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210<br><br>CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; 1st Edition. FDA Standards Recognition # 7-193 | |
| Carryover | To verify carryover. Testing will be performed for WBC, RBC, HGB, and PLT only. | Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells - Carryover (Section 12) | CLSI H26-A2 Validation Verification and Quality Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210 | All carryover testing for WBC, differential, RBC, PLT and Hgb meet the specification with 95% confidence on the upper limit. |
| Detection Capability (Limit Of Blank, Detection And Quantitation) | To assess performance detection capability limits using precision profiles for Lower Limit of Detection (LLoD) and Lower Limit of Quantitation (LLoQ) for WBC, RBC, HGB and PLT measurands. | None | CLSI H26-A2 Validation Verification and Quality Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210<br><br>CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory measurement Procedures; Approved Guideline-second Edition. June 2012. FDA Standards Recognition #7-233 | Results for the detection capability of each instrument for the WBC, RBC, Hgb and Plt parameters were within the specifications. |
| Specimen Stability | To assess specimen stability, two studies were conducted:<br><br>Long term specimen stability assessed the drift in sample value over time at controlled room temperature and at refrigerated temperature. | None | CLSI H26-A2 Validation Verification and Quality Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210 | All parameters met the corresponding requirements for whole blood specimen stability at 8hrs and 24hrs. Results were within the specifications. |

| STUDY | TESTING APPROACH | FDA GUIDANCE DOCUMENTS | STANDARDS/REFERENCES | TESTING RESULTS |
|---|---|---|---|---|
| | Pre-dilute test case will determine the drift in diluted samples over 90 minutes. | | CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents, 1st Edition. FDA Standards Recognition # 7-235 | All parameters met the corresponding requirements for Pre-dilute Stability claim of 15 minutes. |
| Interfering Substances | To determine the level of lipemia, bilirubin, leukocytes and hemoglobin that affects hematology results on the DxH 520. | None | CLSI H26-A2 Validation Verification and Quality Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210<br><br>C56-A Hemolysis, Icterus, and Lipemia/Turbidity Indices as Indicators of Interference in Clinical Laboratory Analysis; Approved Guideline July 2012. FDA Standards Recognition # 7-242 | The concentrations indicated for Lipemia, Conjugated Bilirubin, Unconjugated Bilirubin and Hemoglobin are the highest concentrations that did not interfere with the CBC parameters. For Leucocytes, this is the highest concentration that did not interfere with the Hemoglobin parameter.<br><br>Lipemia: 62.5 mg/dl<br><br>Conjugated Bilirubin: 40mg/dl<br><br>Unconjugated Bilirubin: 20mg/dl<br><br>Hemoglobin: 200 mg/dl<br>Leucocytes:100 x103/uL |
| Equivalency | To demonstrate pre-analytical and within instrument equivalency, three (3) studies were performed:<br><br>Pre-Dilute vs. Whole Blood Sampling Modes<br><br>K2 and K3 EDTA anticoagulant tube types and | None | CLSI H26-A2 Validation Verification and Quality Assurance of Automated Hematology Analyzers - June 2010. FDA Standards Recognition # 7-210<br><br>CLSI GP41-A6 Procedures for the Collection of Diagnostic | In all sampling modes, the results demonstrated equivalency for all parameters tested and performance was within the specifications of the instrument. |

| STUDY | TESTING APPROACH | FDA GUIDANCE DOCUMENTS | STANDARDS/REFERENCES | TESTING RESULTS |
|---|---|---|---|---|
| | site of draw (venous or capillary)<br><br>All sampling modes (Cap Pierce, Open Vial and Tube Holder Open Vial) | | Blood Specimens by Venipuncture; Approved Standard-Sixth Edition. October 2007. FDA Standards Recognition # 7-201<br><br>CLSI GP42-A6 Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard-Sixth Edition. September 2008. FDA Standards Recognition # 7-203 | |
| Reference Intervals | To establish the reference interval for adult males and adult females. Also establish the pediatric reference interval for males and females combined age 0 days – 21 years. | Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells – Reference Values (Section 14) | EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition. October 2010. FDA Standards Recognition # 7-224 | The adult reference interval was established on the DxH520 system for all parameters and included in the product labeling and software. |