



**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY AND INSTRUMENT**

**I Background Information:**

**A 510(k) Number**

K193124

**B Applicant**

Beckman Coulter

**C Proprietary and Established Names**

Unicel DxH 800 Coulter Cellular Analysis System and Unicel DxH 800 Coulter Cellular Analysis System with Early Sepsis Indicator Application

**D Regulatory Information**

| Product Code(s) | Classification | Regulation Section                                                                                                                                         | Panel             |
|-----------------|----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| GKZ             | Class II       | 21 CFR 864.5220 - Automated Differential Cell Counter                                                                                                      | HE - Hematology   |
| QFS             | Class II       | 21 CFR 866.3215 - Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis | MI - Microbiology |

**II Submission/Device Overview:**

**A Purpose for Submission:**

This modification to the DxH 800 is being implemented as part of corrective action for a field action initiated by Beckman Coulter (BEC) in July 2018. The field action was issued on the UniCel DxH 800, DxH 600 and DxH 900 Coulter Cellular Analysis systems to notify customers that BEC identified sporadic erroneously elevated platelet results without flags or system

messages on all software versions. As part of an initial corrective action, BEC developed a software patch that contains an additional criterion to an existing algorithm flag in the software, alerting the user of a suspect PLT finding and to review the result.

The modification is an update to the DxH 800 software to version 3.9.0 which contains the following changes: 1) The addition of a criteria to an existing rule to detect erroneously elevated platelet results caused by sweep flow obstructions; 2) disable the Clear RBC Aperture update; 3) strengthen cybersecurity, and; 4) the addition of an automated VCSn optimization feature.

Note that although the DxH 800 is the subject of this Traditional 510(k), the changes described for software version 3.9.0 will also be applicable to the DxH 600 (software version 1.9.0) and DxH 900 (software version 1.1.1). The DxH 600, CLIA categorized under document CR140130, and the DxH 900, CLIA categorized under document CR180382, are both currently marketed as members of the instrument family of the DxH 800 hematology analyzers in accordance with FDA's Guidance for Industry and FDA Staff, Replacement Reagent and Instrument Family Policy.

#### **B Measurand:**

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.

Monocyte Distribution Width (MDW)

#### **C Type of Test:**

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.

Quantitative assay to measure Monocyte Distribution Width (MDW) parameter

### **III Intended Use/Indications for Use:**

#### **A Intended Use(s):**

See Indications for Use below.

#### **B 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

The Unicel DxH 800 Coulter Cellular Analysis System with Early Sepsis Indicator Application is the quantitative measurement of Monocyte Distribution Width (MDW). The Early Sepsis Indicator is intended for use with adult patients presenting to the emergency department, on whom a white cell differential test has been ordered.

MDW is measured from a (K2EDTA) whole-blood venous sample within 2 hours of collection. MDW values greater than 20.0 together with other laboratory findings and clinical information, aids in identifying patients with sepsis or at increased risk of developing sepsis within the first 12 hours of hospital admission.

MDW values greater than 20.0 should be interpreted in association with other clinical information and diagnostic testing, as a proportion of patients without sepsis may have an elevated MDW value at baseline.

MDW values less than or equal to 20.0 cannot rule out sepsis or the development of sepsis within 12 hours of hospital admission. The Early Sepsis Indicator should not be used as the sole basis to determine the absence of sepsis.

The predictive value of the Early Sepsis Indicator for identifying sepsis in patients with hematological abnormalities has not been established.

#### **C Special Conditions for Use Statement(s):**

Rx - For Prescription Use Only

#### **D Special Instrument Requirements:**

Unicel DxH 800 System (MDW parameter)

### **IV Device/System Characteristics:**

#### **A Device Description:**

The UniCel DxH 800 System contains an automated hematology analyzer (DxH 800) designed for in vitro diagnostic use in screening patient populations by clinical laboratories. The system provides a Complete Blood Count (CBC), Leukocyte 5-Part Differential (Diff), Reticulocyte

(Retic), Nucleated Red Blood Cell (NRBC) on whole blood, as well as, Total Nucleated Count (TNC), and Red Cell Count (RBC) on Body Fluids (cerebrospinal, serous and synovial) and Monocyte Distribution Width (MDW). This parameter has been shown to aid in the early detection of Sepsis in emergency room patients.

The system consists of two primary components, the workstation and the DxH 800 analyzer, the primary function of which is to process samples and provide results to the workstation. The primary functions of the workstation are: user interface, system control, results processing and storage and external communications.

The version of the system proposed in this submission is DxH800 v3.9.0. This system is an update to DxH800 v3.8.0 (see K181599) to: add an automated VCSn optimization feature, which is a software change to verify the Latron CP-X control (beads) recovers within the limits and optimize the calibration factor of the VCSn module; improve cybersecurity; include additional criteria for a flag, and; disable the Clear RBC Apertures function.

## **B Principle 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 use 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.

**C Instrument Description Information:**

| Modes of Operation                                                                                                | Yes                                 | No                                  |
|-------------------------------------------------------------------------------------------------------------------|-------------------------------------|-------------------------------------|
| Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?      | <input checked="" type="checkbox"/> | <input type="checkbox"/>            |
| Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission? | <input type="checkbox"/>            | <input checked="" type="checkbox"/> |
| Software                                                                                                          |                                     |                                     |
| FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types.   | <input checked="" type="checkbox"/> | <input type="checkbox"/>            |

1. Instrument Name:

Unicel DxH 800 Coulter Cellular Analysis System, Unicel DxH 800 Coulter Cellular Analysis System with Early Sepsis Indicator Application

2. Specimen Identification:

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

3. 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).

4. 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.

5. 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.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):

Unicel Dxh 800 Coulter Cellular Analysis System/Unicel Dxh Slidemaker Stainer Coulter Cellular Analysis System, Unicel DxH 800 Cellular Analysis System with Early Sepsis Indicator Application

### B Predicate 510(k) Number(s):

K140911, K181599

### C Comparison with Predicate(s):

| Device & Predicate Device(s):              | <u>K193124</u>                                                                                                                                                                                                        | <u>K140911</u> | <u>K181599</u> |
|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------|
| Device Trade Name                          | Unicel DxH 800 Coulter Cellular Analysis System<br><br>Unicel DxH 800 Coulter Cellular Analysis System with Early Sepsis Indicator Application                                                                        | Same           | Same           |
| General Device Characteristic Similarities |                                                                                                                                                                                                                       |                |                |
| Intended Use / Indications 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 | Same           | Same           |

| Device & Predicate<br>Device(s): | <u>K193124</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | <u>K140911</u> | <u>K181599</u> |
|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------|
|                                  | <p>identifies and enumerates the parameters indicated below on the following sample types:</p> <p>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</p> <p>Pre-Diluted Whole Blood (Venous and Capillary) - WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV</p> <p>Body Fluids (cerebrospinal, serous and synovial) - TNC and RBC</p> <p>The Unicel DxH 800 Coulter Cellular Analysis System with Early Sepsis Indicator Application is the quantitative measurement of Monocyte Distribution Width (MDW). The Early Sepsis Indicator is intended for use with adult patients presenting to the emergency department, on whom a white cell differential test has been ordered.</p> <p>MDW is measured from a (K2EDTA) whole-blood venous sample within 2 hours of collection. MDW values greater than 20.0 together with other laboratory findings and clinical information, aids in identifying patients with sepsis or at increased risk of developing sepsis within the first 12 hours of hospital admission.</p> <p>MDW values greater than 20.0 should be interpreted in association with other clinical information and diagnostic testing, as a proportion of patients without sepsis may have an elevated MDW value at baseline.</p> <p>MDW values less than or equal to 20.0 cannot rule out sepsis or the development of sepsis within 12 hours of hospital admission. The Early Sepsis Indicator should not be used as the sole basis to determine the absence of sepsis.</p> <p>The predictive value of the Early Sepsis Indicator for identifying sepsis in patients with</p> |                |                |

| Device & Predicate Device(s): | <u>K193124</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <u>K140911</u> | <u>K181599</u> |
|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------|
|                               | hematological abnormalities has not been established.                                                                                                                                                                                                                                                                                                                                                                                                                      |                |                |
| Principles of Measurement     | <p>WBC, RBC, MCV, PLT – Aperture impedance (Coulter Principle)</p> <p>Hemoglobin – Spectrophotometric</p> <p>WBC Differential, Reticulocytes, NRBC, MDW – VCSn Technology using:</p> <ul style="list-style-type: none"> <li>• Aperture impedance (DC)</li> <li>• Conductivity (RF)</li> <li>• Laser Light Scatter (Multiple angles)</li> <li>• Laser Light Absorbance</li> </ul>                                                                                           | Same           | Same           |
| Reagents                      | <p><u>Analysis Reagents</u></p> <p>COULTER DxH Diluent</p> <p>COULTER DxH Diff Pack</p> <p>COULTER DxH Cell Lyse</p> <p>COULTER DxH Retic Pack</p> <p>COULTER DxH Cleaner</p> <p><u>Quality Control &amp; Calibrator</u></p> <p>COULTER 6C Cell Control</p> <p>COULTER 6C Plus Cell Control</p> <p>COULTER Latron CP-X Control</p> <p>COULTER RETTC-X Cell Control</p> <p>COULTER LTN-X Control</p> <p>COULTER Body Fluids Control</p> <p>COULTER S-CAL Calibrator kit</p> | Same           | Same           |
| Pre-Analytic Features         | <p><u>System configuration</u></p> <p>PC based workstation running Microsoft Windows XP application specific software</p> <p>Handheld Barcode Scanner Printer</p> <p><u>Sampling Mechanism</u></p> <p>Single tube presentation - open and closed vial sampling.</p> <p>Automated presentation - closed vial sampling from 5 position cassette; Maximum initial load capacity 20 racks</p>                                                                                  | Same           | Same           |

| Device & Predicate<br>Device(s): | <u>K193124</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <u>K140911</u> | <u>K181599</u> |
|----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------|
|                                  | <p><u>Mechanisms for processing</u><br/>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.</p> <p>Cassette transportation by magnetic drive allowing multi-directional moves and capability to return cassette to Sampling position for repeat / reflex testing.</p> <p><u>Sample identification</u><br/>Sample aspiration module (SAM) mounted barcode reader for automated barcode reading of cassette and sample tube identifiers<br/>Manual barcode scanning of sample tube identifier (Handheld scanner)<br/>Manual keyboard entry of sample identifier</p> |                |                |
| Sample Processing                | <p><u>Aspiration Pathway</u><br/>Single sampling probe and common aspiration pathway used for all sample presentation modes.</p> <p><u>Sample aspiration volume</u><br/>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</p> <p><u>Throughput</u><br/>For automatic mode:</p> <ul style="list-style-type: none"> <li>• CBC at 100 specimens/hr.</li> <li>• CBC and Differential at 100 specimens/hr.</li> <li>• CBC and Differential with NRBC at 90 specimens/hr.</li> <li>• Retic at 45 specimens/hr.</li> </ul> <p><u>Data reporting</u><br/>Workstation display graphics, hardcopy printing and transmission to Laboratory Information System (LIS)</p>                             | Same           | Same           |

| Device & Predicate Device(s):                    | <u>K193124</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <u>K140911</u> | <u>K181599</u> |
|--------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------|
| System Control and Software                      | <p><u>Controlling software</u><br/>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 resident in the Workstation.</p> <p>In addition, an Embedded Application is resident in the analyzer. The Embedded application uploads from the workstation on system power-up.</p> <p>Extensive real time monitoring and reporting of system status including:<br/>Component and module activities,</p> <ul style="list-style-type: none"> <li>• System Voltages and Currents</li> <li>• System Pressure and Vacuum</li> <li>• System Temperatures</li> <li>• Motor activity</li> <li>• Mechanism Sensor status</li> <li>• Reagent Pump Operation</li> </ul> <p>Raw data collection, Single sampling probe and common aspiration pathway used for all sample presentation modes.</p> | Same           | Same           |
| <b>General Device Characteristic Differences</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                |                |
| Software Version                                 | <p>Version 3.9.0</p> <ul style="list-style-type: none"> <li>• Includes the additional criteria for a flag</li> <li>• Disable Clear RBC Aperture</li> <li>• Strengthened Cybersecurity</li> <li>• Automated VCSn Optimization</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Version 3.8.0  | Version 3.8.0  |

## VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition.

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

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

CLSI EP09c, Measurement Procedure Comparison and Bias Estimation Using Patient Samples - Third Edition.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

#### 1. Precision/Reproducibility:

##### **Precision (Sample Repeatability) – PLT**

The objective of the study was to assess system precision (sample repeatability) for the PLT parameter on the modified DxH 800 system. The study evaluated the repeatability of whole blood measurements across the low, normal, and high ranges for the PLT parameter. Studies were conducted according to CLSI EP05-A3.

Data was generated using the instrument's repeatability and closed-vial sampling modes. Fresh whole blood specimens within 8 hours of collection with a minimum of 1 mL volume remaining were used for this testing. The study was executed with two instruments (DxH 800 (Test A) and DxH 800 (Test B)) at one internal BEC site. Within-run repeatability of the PLT parameter was performed using 10 aspirations of normal whole blood samples collected in K2EDTA. Three samples within each range were tested on each instrument. When possible, additional runs were collected to compensate for flagged runs. With some abnormal blood samples, where the volume obtained for testing may be less than the required amount to obtain 10 replicates, a second sample was analyzed for the same parameter and range. One run was excluded on one instrument for insufficient quantity for one of the three low range samples. Mean and CV% were reported for each sample automatically from the instrument.

All PLT results met the precision (sample repeatability) specifications. There was no impact to PLT precision on the DxH 800 from the software design change implementing the additional criteria for a flag (Change 1) and disabling the Clear RBC Procedure (Change 2).

##### **Repeatability – Test A**

| <b>Platelet Range</b> | <b>Concentration</b> | <b>N</b> | <b>Test Result Mean</b> | <b>Test Result %CV</b> |
|-----------------------|----------------------|----------|-------------------------|------------------------|
| Low                   | >15.0 to <200.0      | 10       | 172.5                   | 1.77                   |
| Low                   | >15.0 to <200.0      | 10       | 133.8                   | 2.2                    |
| Low                   | >15.0 to <200.0      | 10       | 189.8                   | 1.78                   |
| Normal                | 200.00 to 400.00     | 10       | 321.9                   | 1.8                    |
| Normal                | 200.00 to 400.00     | 10       | 301.6                   | 2.04                   |

| Platelet Range | Concentration      | N  | Test Result Mean | Test Result %CV |
|----------------|--------------------|----|------------------|-----------------|
| Normal         | 200.00 to 400.00   | 10 | 331.5            | 2.09            |
| High           | >400.0 to 3,000.00 | 10 | 418.3            | 2.26            |
| High           | >400.0 to 3,000.00 | 10 | 499.8            | 2.4             |
| High           | >400.0 to 3,000.00 | 10 | 449.2            | 1.33            |

#### Repeatability – Test B

| Platelet Range | Concentration      | N  | Test Result Mean | Test Result %CV |
|----------------|--------------------|----|------------------|-----------------|
| Low            | >15.0 to <200.0    | 9  | 98.5             | 2.09            |
| Low            | >15.0 to <200.0    | 10 | 170.2            | 1.42            |
| Low            | >15.0 to <200.0    | 10 | 163.5            | 1.74            |
| Normal         | 200.00 to 400.00   | 10 | 319.6            | 1.14            |
| Normal         | 200.00 to 400.00   | 10 | 340.6            | 1.6             |
| Normal         | 200.00 to 400.00   | 10 | 311.6            | 1.89            |
| High           | >400.0 to 3,000.00 | 10 | 463.6            | 1.51            |
| High           | >400.0 to 3,000.00 | 10 | 464.9            | 0.94            |
| High           | >400.0 to 3,000.00 | 10 | 511.3            | 1.38            |

#### System Precision (Sample Repeatability) – Change 4

The objective of the study was to assess system precision (sample repeatability) for the parameters measured directly or derived through histogram on the DxH 800 version 3.9.0 system inclusive of all software design changes (includes the automated VSCn Optimization (Change 4)). The study evaluated the customer use validation of repeatability as described in the Instructions for Use (IFU) for whole blood measurements across the low, normal and high ranges for parameters measured directly or derived through histogram (WBC, RBC, Hgb, MCV, RDW, RDW-SD, PLT, MPV, LY%, MO%, NE%, EO%, BA%, NRBC, Reticulocyte %, IRF and MRV). Studies were conducted according to CLSI EP05-A3.

Data was generated using the instrument's repeatability and closed-vial sampling modes. Fresh whole blood specimens within 8 hours of collection with a minimum of 1 mL volume remaining were used for this testing. The study was executed with two instruments (Test A and Test B) at one internal BEC site. Within-run repeatability of the parameters was performed using 10 aspirations of normal whole blood samples collected in K2EDTA. A single sample within each range was tested on each instrument. When sufficient sample volume existed, the same sample was used across instruments. For MDW, a sample close to the cut-off (20) was chosen to test the sample repeatability. When possible, additional runs were collected to compensate for flagged runs. With some abnormal blood samples, where the volume obtained for testing may be less than the required amount to obtain 10 replicates,

a second sample was analyzed for the same parameter and range. Two runs were excluded due to partial aspiration for the Retic parameter. Mean and %CV were reported for each sample automatically from the instrument.

#### Repeatability – Test A

| Parameter | N   | Test Result Mean | Test Result %CV or SD |
|-----------|-----|------------------|-----------------------|
| WBC       | 10  | 5.873            | 2.02%                 |
| RBC       | 10  | 4.721            | 0.9%                  |
| Hgb       | 10  | 15.47            | 1.12%                 |
| MCV       | 10  | 88.18            | 0.32%                 |
| RDW %     | 10  | 13.09            | 0.8%                  |
| RDW-SD    | 10  | 40.25            | 1.0%                  |
| Platelet  | 10  | 230.4            | 3.3%                  |
| MPV       | 10  | 8.32             | 1.03%                 |
| Neut %    | 10  | 58.99            | 1.21%                 |
| Lymph %   | 10  | 31.12            | 1.34%                 |
| Mono %    | 10  | 9.89             | 3.01%                 |
| Eos %     | 10  | 3.42             | 4.4%                  |
| Baso %    | 10  | 0.64             | 0.16 SD               |
| NRBC      | NA  | N/A              | N/A                   |
| NRBC      | 10  | 4.27             | 19.68%                |
| NRBC      | N/A | NA               | N/A                   |
| Retic %   | 10  | 0.701            | 0.06 SD               |
| Retic %   | 10  | 3.08             | 0.21 SD               |
| Retic %   | 9   | 4.23             | 3.60%                 |
| IRF       | 10  | 0.282            | 16.16%                |
| MRV       | 10  | 107.94           | 1.42%                 |
| MDW       | 10  | 18.97            | 4.06%                 |

#### Repeatability – Test B

| Parameter | N  | Test Result Mean | Test Result %CV or SD |
|-----------|----|------------------|-----------------------|
| WBC       | 10 | 6.092            | 1.08%                 |

| Parameter | N   | Test Result Mean | Test Result %CV or SD |
|-----------|-----|------------------|-----------------------|
| RBC       | 10  | 4.926            | 0.62%                 |
| Hgb       | 10  | 14.98            | 0.7%                  |
| MCV       | 10  | 86.52            | 0.43%                 |
| RDW %     | 10  | 13.96            | 0.88%                 |
| RDW-SD    | 10  | 43.66            | 1.48%                 |
| Platelet  | 10  | 323.8            | 1.18%                 |
| MPV       | 10  | 8.18             | 1.21%                 |
| Neut %    | 10  | 58.81            | 0.88%                 |
| Lymph %   | 10  | 30.69            | 1.65%                 |
| Mono %    | 10  | 6.66             | 2.49%                 |
| Eos %     | 10  | 2.87             | 3.13%                 |
| Baso %    | 10  | 0.96             | 0.29 SD               |
| NRBC      | N/A | N/A              | N/A                   |
| NRBC      | 10  | 2.09             | 10.15%                |
| NRBC      | N/A | N/A              | N/A                   |
| Retic %   | 10  | 0.926            | 0.06 SD               |
| Retic %   | 10  | 2.013            | 0.12 SD               |
| Retic %   | 9   | 4.222            | 3.10%                 |
| IRF       | 10  | 0.468            | 5.79%                 |
| MRV       | 10  | 117.96           | 1.23%                 |
| MDW       | 10  | 20.55            | 5.26%                 |

#### **System Precision (Sample Repeatability) – Change 4 with daily shutdown cycles (additional precision study)**

The objective of the study was to assess system precision (sample repeatability) for the parameters measured directly or derived through histogram on the DxH 800 version 3.9.0 system inclusive of all software design changes (includes the automated VSCn Optimization (Change 4)). To verify repeatability for all parameters except MDW, three runs with 10 replicates of the same sample were tested, including a Latron CP-X control run for each set. After each run, the daily shutdown cycle was performed. To verify repeatability for the MDW parameter, two runs with 10 replicates of the same sample were tested including a Latron CP-X control run for each set, performed within the 2-hour stability claim. After each run, the daily shutdown cycle was performed.

Data was generated using the instrument's repeatability and closed-vial sampling modes. Fresh whole blood specimen collected within 24 hours were used for this testing. For the MDW parameter, specimens were processed within 30 minutes of collection. The study was executed with two instruments at one internal BEC site. For each calibration adjustment cycle which included the Automated VSCn Optimization change, within-run repeatability was performed using 10 aspirations of normal whole blood samples collected in K2EDTA for all parameters except for NRBC where 6C Control Level 2 was used for the 2–15 range and Retic-X Cell Control Level 3 was used for the Retic 4–15 range.

Three sets of analyses were completed for all parameters except for MDW within 24 hours of collection. For MDW, two sets of analyses were performed within 2 hours from blood collection. Each data set is inclusive of one instrument calibration cycle. The instrument calibration cycle consists of a Shutdown, Startup, Daily Checks and Latron CP-X Control. The sequence for the three sets of analyses were as follows:

- Shutdown 1, Startup, Daily Checks, Latron CP-X Control 1, Precision Set 1
- Shutdown 2, Startup, Daily Checks, Latron CP-X Control 2, Precision Set 2
- Shutdown 3, Startup, Daily Checks, Latron CP-X Control 3, Precision Set 3

For MDW, two sets of analysis were performed within 2 hours from blood collection inclusive of two instrument calibration adjustment cycles. The sequence for the two sets of analyses were as follows:

- Shutdown 1, Startup, Daily Checks, Latron CP-X Control 1, Precision Set 1
- Shutdown 2, Startup, Daily Checks, Latron CP-X Control 2, Precision Set 2

For each repeatability dataset, the mean, SD and CV% were reported for each parameter where the mean represents the range while SD or CV% the repeatability performance. All parameters met the precision (sample repeatability) specifications.

## 2. Linearity:

The objective of the study was to evaluate linearity measurands on the DxH 800 version 3.9.0 system inclusive of the software design changes in accordance with CLSI EP06-A. 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. Linearity was performed on three instruments located at a BEC internal testing site, using one dilution series per measurand to cover the Analytical Measuring Interval (AMI). Four replicates of each dilution were analyzed in random order. Replicates 2 through 4 were used for the analysis.

Fresh whole blood was obtained and concentrated to achieve high starting values near the upper limit of the AMI for the RBC and Hgb parameters. WBC and PLT linearity used cell analogs and media material. Dilutions were prepared to cover the AMI for each parameter and analyzed in quadruplicate in random order. There were four WBC results exclusions (3 partial aspirations and 1 with an "R" flag).

Data were analyzed including all dilution points for each parameter. Linearity was evaluated by fitting linear and non-linear (quadratic and cubic) models and assessing that the deviations

from linearity (difference between the non-linear and linear fits) were within acceptance criteria. WBC, RBC, Hgb, and PLT parameters met the linearity specifications.

3. Analytical Specificity/Interference:

Refer to 510(k) cleared device: K102771

4. Assay Reportable Range:

Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Refer to 510(k) cleared device: K140911

6. Detection Limit:

Refer to 510(k) cleared device: K140911

7. Assay Cut-Off:

Not applicable

8. Accuracy (Instrument):

Not applicable

9. Carry-Over:

The objective of the study was to evaluate specimen carryover on the DxH 800 version 3.9.0 system inclusive of the software design changes. The study assessed the impact of a specimen with high target value (HTV) preceding a low target value sample (LTV). Carryover was evaluated in accordance with CLSI H26-A2.

Testing was performed on three instruments, at an internal BEC site, using the instrument's carryover mode, in closed vial sampling mode and used whole blood specimens. Testing was performed for high WBC, RBC, Hgb, and PLT. Low target value samples (LTV) were diluted (a small amount of whole blood was added to particle-free plasma) to achieve the desired range. All samples were concentrated to achieve the high target values (HTV) for WBC, RBC, PLT and HGB. In addition, analogs were used to achieve WBC HTV > 300.

The target number for each measurand was three sets for each parameter on all three instruments to assure the minimum number was achieved. The same donor was used across all three instruments. Different donors were used for each parameter.

Carryover was calculated as follows:

$$\% \text{ carryover} = [(LTV_1 - LTV_3) / (HTV_3 - LTV_3)] \times 100,$$

Where *HTV* is the high whole blood specimen and *LTV* is the low whole blood specimen.

The carryover by parameter for each system was calculated. All carryover testing (by sample and overall) for WBC, RBC, Hgb and PLT passed. The WBC and RBC carryover testing were <0.5%, meeting the acceptance limit. PLT and Hgb also met the requirement of carryover. Carryover specifications were not impacted by the DxH 800 version 3.9.0 software design changes.

## B Comparison Studies:

### 1. Method Comparison with Predicate Device:

#### Method Comparison (Change 1 & Change 2)

The objective of the study was to support substantial equivalence by comparison of the PLT values obtained on the DxH 800 system version 3.9.0, including the additional criteria for a flag (Change 1) and the disabled Clear RBC Procedure (Change 2), to the values obtained on the predicate device, DxH 800 version 3.0.0 (K140911). The predicate device software does not include the additional criteria for a flag nor the clear RBC procedure.

A total of 127 whole blood specimens (27 normal, 100 clinical) collected in K2EDTA were included in the study. Specimens were less than 24 hours old from the time of draw and were targeted to cover the AMI for the PLT parameter. The CBC calibration of instruments was verified prior to the start of testing and each day that testing occurred. Verification was met and no adjustments made to the calibration of any instrument. The measurement procedure comparison paired study design was performed with two test systems (Test A and Test B) and one predicate system at one site with varying clinical samples.

Basic summary statistics and Bland-Altman plots were calculated for PLT. The Weighted Deming approach was used to estimate PLT regression. Weighted Deming approach was used for PLT because the variability (scatter) of the data depended on the range of measurements. Regression analysis was performed using replicate 1 of the test vs. replicate 1 of the comparator. Bias between methods was calculated from the regression line at the 25<sup>th</sup>, 50<sup>th</sup>, and 75<sup>th</sup> percentile of the range and at medical decision points. Confidence limits were calculated based on standard errors and 95% confidence. The upper/lower confidence limits were compared to the Acceptance Limits.

### Regression Statistics and Correlation

#### Test A

|         |                          |       | 95% Confidence Limits |       |           | 95% Confidence Limits |       |             |
|---------|--------------------------|-------|-----------------------|-------|-----------|-----------------------|-------|-------------|
| Analyte | Unit                     | Slope | Lower                 | Upper | Intercept | Lower                 | Upper | Correlation |
| PLT     | 10 <sup>3</sup> cells/uL | 1.041 | 1.033                 | 1.050 | -0.242    | -1.019                | 0.536 | 0.998       |

#### Test B

|         |                          |       | 95% Confidence Limits |       |           | 95% Confidence Limits |       |             |
|---------|--------------------------|-------|-----------------------|-------|-----------|-----------------------|-------|-------------|
| Analyte | Unit                     | Slope | Lower                 | Upper | Intercept | Lower                 | Upper | Correlation |
| PLT     | 10 <sup>3</sup> cells/uL | 0.989 | 0.983                 | 0.995 | 0.216     | -0.462                | 0.895 | 0.999       |

### **Method Comparison (Change 4)**

The objective of the study was to support substantial equivalence of the DxH 800 system version 3.9.0 (automated VSCn Optimization - Change 4) to the predicate device, DxH 800 version 3.8.0 (K181599) by comparing parameters measured directly or derived through histogram.

A total of 224 whole blood specimens (40 normal, 184 clinical) collected in a K2EDTA were included in this study covering the AMI for the parameters measured. The CBC calibration of instruments was verified prior to the start of testing and each day that testing occurred.

Verification was met and no adjustments were made to the calibration of any instrument. The measurement procedure comparison paired study design was performed with two test systems (Test A and Test B) and one predicate system at one site with varying clinical samples.

Basic summary statistics and Bland-Altman plots were calculated for each parameter. The Deming approach was used to estimate regression parameters. Weighted Deming approach was used for cell counts parameters because the variability (scatter) of the data depended on the range of measurements. Regression analysis was performed using replicate 1 of the test vs. replicate 1 of the comparator. Bias between methods was calculated from the regression line at the 25<sup>th</sup>, 50<sup>th</sup>, and 75<sup>th</sup> percentile of the range and at medical decision points. Confidence limits were calculated based on standard errors and 95% confidence. The upper/lower confidence limits were compared to the instrument accuracy claim. Estimated biases and their 95% confidence limits for the 25<sup>th</sup>, 50<sup>th</sup>, and 75<sup>th</sup> percentiles and medical decision levels were calculated for each test instrument against the same comparator.

### **Regression Statistics and Correlation**

#### **Test A**

|         |                          |       | 95% Confidence Limits |       |           | 95% Confidence Limits |        |             |
|---------|--------------------------|-------|-----------------------|-------|-----------|-----------------------|--------|-------------|
| Analyte | Unit                     | Slope | Lower                 | Upper | Intercept | Lower                 | Upper  | Correlation |
| WBC     | 10 <sup>3</sup> cells/uL | 0.985 | 0.978                 | 0.992 | 0.010     | -0.022                | 0.041  | 1.000       |
| RBC     | 10 <sup>6</sup> cells/uL | 0.992 | 0.987                 | 0.997 | 0.027     | 0.011                 | 0.043  | 0.999       |
| HGB     | g/dL                     | 0.998 | 0.993                 | 1.003 | -0.031    | -0.081                | 0.019  | 0.999       |
| MCV     | fL                       | 0.998 | 0.989                 | 1.007 | 0.678     | -0.090                | 1.446  | 0.998       |
| RDW     | %                        | 1.014 | 1.001                 | 1.027 | -0.240    | -0.445                | -0.035 | 0.997       |
| RDWSD   | fL                       | 1.007 | 0.993                 | 1.022 | -0.593    | -1.296                | 0.110  | 0.995       |
| PLT     | 10 <sup>3</sup> cells/uL | 1.039 | 1.031                 | 1.046 | 0.259     | -0.593                | 1.110  | 0.999       |
| MPV     | fL                       | 0.985 | 0.947                 | 1.022 | 0.165     | -0.152                | 0.482  | 0.969       |
| NE      | %                        | 1.002 | 0.994                 | 1.010 | -0.179    | -0.763                | 0.405  | 0.999       |
| LY      | %                        | 1.007 | 0.996                 | 1.019 | -0.043    | -0.263                | 0.177  | 0.998       |
| MO      | %                        | 0.996 | 0.979                 | 1.013 | -0.042    | -0.189                | 0.104  | 0.997       |
| EO      | %                        | 0.977 | 0.935                 | 1.019 | 0.005     | -0.086                | 0.096  | 0.996       |
| BA      | %                        | 1.478 | 0.982                 | 1.975 | -0.247    | -0.512                | 0.019  | 0.705       |
| NRBC    | per 100 WBC              | 1.008 | 0.882                 | 1.133 | -0.015    | -0.055                | 0.026  | 0.987       |
| RET     | %                        | 0.992 | 0.953                 | 1.031 | -0.062    | -0.124                | -0.001 | 0.990       |
| MRV     | fL                       | 0.966 | 0.934                 | 0.998 | 3.026     | -0.705                | 6.757  | 0.977       |
| IRF     | N/A                      | 0.969 | 0.907                 | 1.030 | 0.018     | -0.012                | 0.048  | 0.935       |

### Test B

|         |                          |       | 95% Confidence Limits |       |           | 95% Confidence Limits |       |             |
|---------|--------------------------|-------|-----------------------|-------|-----------|-----------------------|-------|-------------|
| Analyte | Unit                     | Slope | Lower                 | Upper | Intercept | Lower                 | Upper | Correlation |
| WBC     | 10 <sup>3</sup> cells/uL | 1.001 | 0.996                 | 1.006 | 0.003     | -0.014                | 0.020 | 1.000       |
| RBC     | 10 <sup>6</sup> cells/uL | 1.011 | 1.000                 | 1.023 | -0.003    | -0.042                | 0.037 | 0.999       |
| HGB     | g/dL                     | 1.006 | 1.001                 | 1.011 | 0.006     | -0.042                | 0.054 | 0.999       |
| MCV     | fL                       | 0.987 | 0.980                 | 0.993 | 1.020     | 0.424                 | 1.617 | 0.999       |
| RDW     | %                        | 0.999 | 0.984                 | 1.014 | -0.025    | -0.261                | 0.212 | 0.996       |
| RDWSD   | fL                       | 1.003 | 0.986                 | 1.020 | -0.117    | -0.929                | 0.695 | 0.994       |
| PLT     | 10 <sup>3</sup> cells/uL | 1.000 | 0.994                 | 1.007 | -0.301    | -1.130                | 0.528 | 0.999       |
| MPV     | fL                       | 0.984 | 0.940                 | 1.029 | 0.122     | -0.251                | 0.494 | 0.973       |
| NE      | %                        | 1.001 | 0.992                 | 1.010 | -0.233    | -0.911                | 0.446 | 0.998       |
| LY      | %                        | 1.006 | 0.994                 | 1.018 | 0.086     | -0.140                | 0.312 | 0.998       |
| MO      | %                        | 1.000 | 0.984                 | 1.017 | -0.091    | -0.227                | 0.046 | 0.996       |
| EO      | %                        | 0.974 | 0.923                 | 1.025 | 0.039     | -0.070                | 0.147 | 0.995       |
| BA      | %                        | 1.123 | 0.814                 | 1.432 | -0.027    | -0.185                | 0.131 | 0.676       |
| NRBC    | per 100 WBC              | 1.003 | 0.885                 | 1.122 | -0.008    | -0.049                | 0.032 | 0.985       |
| RET     | %                        | 1.053 | 1.007                 | 1.099 | -0.064    | -0.136                | 0.009 | 0.992       |
| MRV     | fL                       | 1.009 | 0.971                 | 1.048 | -1.697    | -6.152                | 2.758 | 0.973       |
| IRF     | N/A                      | 0.978 | 0.929                 | 1.027 | 0.004     | -0.020                | 0.028 | 0.945       |

### Measurement Procedure Comparison to Predicate device (DxH 800 v 3.8) for MDW – Change 4

The objective of the study was to support substantial equivalence by comparison of the MDW values obtained on the DxH 800 system version 3.9.0, (automated VSCn Optimization (Change 4)) to the values obtained on the predicate device, DxH 800 version 3.8.0 (K181599).

A total of 107 whole blood specimens (18 normal, 89 clinical) collected in in K2EDTA comprised of normal specimens obtained from the in-house donor program, and clinical specimens obtained from spent hospital samples, meeting the following criteria:

- Normal: 4 – 24 hours old stored at room temperature
- Abnormal: 4 – 24 hours old. Defined as native samples from ambulatory subjects. Use for MDW range coverage 20 – 25+

Regression analysis was performed using replicate 1 of the test instrument versus replicate 1 of the comparator instrument. Basic summary statistics and Bland-Altman plots were calculated. Deming approach was used to estimate regression parameters. Bias was calculated at 50<sup>th</sup> percentile point and cut-off levels when appropriate. Confidence limits were calculated based on standard errors and 95% confidence. The upper/lower confidence limits were compared to the Acceptance Limits. The 50<sup>th</sup> percentile and cut-off levels (near 20) correspond to the cut-off point for the early detection of Sepsis. MDW comparability results met the specifications.

## Regression Statistics and Correlation (MDW)

|               |       | 95% Confidence Limits |       |           | 95% Confidence Limits |       |             |
|---------------|-------|-----------------------|-------|-----------|-----------------------|-------|-------------|
|               | Slope | Lower                 | Upper | Intercept | Lower                 | Upper | Correlation |
| <b>Test A</b> | 1.023 | 0.899                 | 1.148 | -0.385    | -3.013                | 2.242 | 0.952       |
| <b>Test B</b> | 1.029 | 0.910                 | 1.147 | -0.388    | -2.895                | 2.120 | 0.948       |

### 2. Matrix Comparison:

Refer to 510(k) cleared device: K120771

## C Clinical Studies:

### 1. Clinical Sensitivity:

Refer to 510(k) cleared device: K120771

### 2. Clinical Specificity:

Refer to 510(k) cleared device: K120771

### 3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Refer to 510(k) cleared devices: K120771 and K140911

## D Clinical Cut-Off:

Not applicable

## E Expected Values/Reference Range:

Refer to 510(k) cleared device: K120771

## F Other Supportive Instrument Performance Characteristics Data:

Refer to 510(k) cleared devices: K120771 and K140911

## Retrospective Data Analysis

The objective was to conduct a retrospective data analysis using data obtained during the investigation to determine the flagging rates of erroneous PLT events before and after the addition of the flagging criteria. The study involved comparison of erroneously elevated platelet event rates in pre- and post- release of the additional platelet flagging criteria on the DxH 800/600 software.

Sample runs on 678 DxH 800/600 instruments (connected to BEC via ProService) containing the platelet flagging criteria software were analyzed. The calculated results and flags from runs on these instruments were evaluated for the presence of the low-end platelet interference flag (PLT Inter: Debris) pre- and post- installation of the flagging criteria software. Pre- and Post- software release event rates were compared to each other and the difference between event rates was normally distributed and the standardized zscore was calculated.

The retrospective data analysis demonstrated the flagging rate remained statistically unchanged with or without the addition of the additional platelet flagging criteria.

## **VIII Proposed Labeling:**

The labeling supports the finding of substantial equivalence for this device.

## **IX Conclusion:**

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