

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k140911

B. Purpose for Submission:

Software update for UniCel[®] DxH 800 and DxH Slidemaker Stainer (SMS) COULTER[®] Cellular Analysis System to software version 3.0 to consolidate control of up to three DxH 800 instruments and one DxH SMS arranged in the workcell configuration. Includes hardware modifications (fasteners) to physically connect the components of the workcell together on and a server to host the workstation software.

C. Manufacturer and Instrument Name:

Beckman Coulter, Inc.; UniCel[®] DxH 800 COULTER[®] Cellular Analysis System; UniCel[®] DxH Slidemaker Stainer COULTER[®] Cellular Analysis System

D. Type of Test or Tests Performed:

Quantitative test for WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, NE%, NE#, LY%, LY#, MO%, MO#, EO%, EO#, BA%, BA#, NRBC%, NRBC#, RET%, RET#, MRV, IRF, and body fluid (TNC and RBC) parameters.

E. System Descriptions:

1. Device Description:

DxH 800: The UniCel DxH 800 Analyzer is a quantitative, automated hematology analyzer for in vitro diagnostic use in screening patient populations found in clinical laboratories. The UniCel DxH 800 Analyzer provides a Complete Blood Count (CBC), Leukocyte Five-part Differential (Diff), Reticulocyte (RET), Nucleated Red Blood Cell (NRBC) on whole blood, Total Nucleated Count (TNC) and Red Blood Cell Count (RBC) on Body Fluids (cerebrospinal, serous and synovial).

DxH SMS: The DxH Slidemaker Stainer is a fully automated slide preparation and staining device that aspirates a whole-blood sample, smears a blood film on a clean microscope slide, and delivers a variety of fixatives, stains, buffers, and rinse solutions to that blood smear.

The upgrade of these devices with software v3.0 allows for these stand-alone devices to be configured into five workcell configurations through physical and virtual connections. Physically, the instruments are connected via hardware and the virtual connection is

accomplished by means of the new control system software that provides integrated process control, data consolidation and sample transport to the various instruments in the workcell allowing parallel specimen processing or instrument dedication to a specialized suite of tests. This will yield a total of seven product configurations, including:

- Stand-alone DxH 800 with software v3.0
- Stand-alone DxH SMS with software v3.0
- Five customizable workcell configurations comprised of DxH 800 and DxH SMS with software v3.0
 - DxH 801 – one DxH 800 + one DxH SMS
 - DxH 1600 – two DxH 800
 - DxH 1601 – two DxH 800 + one DxH SMS
 - DxH 2400 – three DxH 800
 - DxH 2401 – three DxH 800 + one DxH SMS

2. Principles of Operation:

This updated version of the DxH 800 utilizes the same principles of operation, reagents, controls and calibrators as the original cleared device.

Refer to 510(k) cleared device: k120771

3. Modes of Operation:

Refer to 510(k) cleared device: k120771

4. Specimen Identification:

Refer to 510(k) cleared device: k120771

5. Specimen Sampling and Handling:

Refer to 510(k) cleared device: k120771

6. Calibration:

Refer to 510(k) cleared device: k120771

7. Quality Control:

Refer to 510(k) cleared device: k120771

8. Software:

FDA has reviewed applicant's Hazard Analysis and Software Development processes for this line of product types:

Yes ___X___ or No _____

F. Regulatory Information:

1. Regulation section:

21 CFR § 864.5220, Automated differential cell counter

2. Classification:

Class II

3. Product code:

GKZ, Counter, differential cell

4. Panel:

Hematology (81)

G. Intended Use:

1. Indication(s) for Use:

DxH 800

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

DxH SMS

The DxH Slidemaker Stainer is a fully automated slide preparation and staining device that aspirates a whole-blood sample, smears a blood film on a clean microscope slide, and delivers a variety of fixatives, stains, buffers, and rinse solutions to that blood smear.

2. **Special Conditions for Use Statement(s):**

For prescription use only

H. Substantial Equivalence Information:

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

UniCel[®] DxH 800 COULTER[®] Cellular Analysis System; k120771

2. **Comparison with Predicate Device:**

DxH 800 (v3.0 versus v2.0) Device Comparison Table:

Similarities		
Item	Device: UniCel [®] DxH 800 Update (Software 3.0)	Predicate: UniCel [®] DxH 800 (Software 2.0)
Indications for use	<p>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.</p> <p>The UniCel[®] DxH 800 Analyzer identifies and enumerates the parameters indicated below on the following sample types:</p> <ul style="list-style-type: none"> • 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, 	Same

Similarities		
Item	Device: UniCel [®] DxH 800 Update (Software 3.0)	Predicate: UniCel [®] DxH 800 (Software 2.0)
	MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV • Body Fluids (cerebrospinal, serous and synovial) – TNC and RBC	
Sampling Mechanism	<ul style="list-style-type: none"> • Single aspiration probe used for all sampling. • Single tube presentation – open and closed vial sampling – specimen manually mixed • Automated cassette presentation – closed vial sampling from five-position cassette accepting a variety of defined specimen tubes. Cassette containing specimens mixed prior to starting sampling and between specimens. • Maximum initial load capacity 20 cassettes - System will continuously process cassettes as added. 	Same
Mechanisms for Processing	Mechanisms to achieve process of: <ul style="list-style-type: none"> • 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 • data reporting Specimen tube is in upright (cap up) position for closed vial sampling Cassette transportation by magnetic drive allowing multi-directional moves and capability to return cassette to sampling position for repeat / reflex testing	Same
Data Analysis	Raw information is digitized from all analytical modules and passed to workstation for algorithmic processing. Algorithms using advanced mathematical methods for population differentiation and flagging centralized within workstation	Same
Data Reporting	Workstation display graphics, hardcopy printing and transmission to host Laboratory Information System (LIS)	Same
Performance Characteristics	The performance characteristics provided for: <ul style="list-style-type: none"> • Comparison of Measurement Procedures 	Same

Similarities		
Item	Device: UniCel[®] DxH 800 Update (Software 3.0)	Predicate: UniCel[®] DxH 800 (Software 2.0)
	<ul style="list-style-type: none"> • Whole Blood – CBC • Whole Blood - Reticulocyte • Whole Blood – Differential • Whole Blood – NRBC • Body Fluids • Imprecision <ul style="list-style-type: none"> • Whole Blood CBC, DIFF, Retic • Prediluted Blood • CSF, Serous, Synovial Body Fluid • Linearity • Carryover (High to Low) <ul style="list-style-type: none"> • Whole Blood CBC, DIFF, Retic, NRBC • Body Fluids 	
Operating Principles	Method of sample analysis	Same
Consumables	Reagents, controls, and calibrators utilized by the system	Same

Differences		
Item	Device: UniCel[®] DxH 800 Update (Software 3.0)	Predicate: UniCel[®] DxH 800 (Software 2.0)
System Configuration	<p>Individual analyzers are same as predicate except analyzers can be connected creating multiple workcell configurations (up to three DxH 800s and up to 1 DxH SMS)</p> <p>Workcell configurations available only on a floor stand, not on a bench top.</p> <p>PC based workstation running Microsoft Windows 7 application specific software</p>	<ul style="list-style-type: none"> • Workcell configuration of one DxH 800 (stand-alone) • Bench top • Optional Floor Stand provides self-contained support for the analyzer as well as easy access storage for reagents and waste containers. <p>PC based workstation running Microsoft Windows XP application specific software.</p>
Workstation	Each DxH 800 in the workcell utilizes the same functionality as the predicate except one system manager controls sample processing and management for up to three DxH 800s plus one DxH SMS	Software functionality to control sample processing as well as patient and control data management

DxH Slidemaker Stainer (SMS) Device Comparison Table:

Item	Device: UniCel [®] DxH SMS (Software 3.0)	Predicate: WBC Manual Differential Method (CLSI H20-A2)
Indications for use	The DxH Slidemaker Stainer is a fully automated slide preparation and staining device that aspirates a whole blood sample, smears a blood film on a clean microscope slide, and delivers a variety of fixatives, stains, buffers, and rinse solutions to that blood smear.	Manual preparation of whole blood smears on microscopic slides using a variety of fixatives, stains, buffers, and rinse solutions.
Specimen Collection	Whole venous blood in EDTA	Same
Blood Film Preparation	Automatically prepared by DxH SMS	Manually prepared by technician
Blood Film Requirements	Section 6.3.1 of CLSI H20-A2	Same

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

Class II Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells; Final Guidance for Industry and FDA

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

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

CLSI H20-A2, Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard-Second Edition

CLSI EP09-A3, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition

J. Performance Characteristics

1. Analytical Performance:

The DxH 800 and DxH SMS v3.0 test strategy was designed to evaluate the software changes and minor hardware changes made and the effect of those changes on analytical

performance. The scope of the software changes is limited to the workstation software and the hardware changes only impacted the physical connection of the instruments together. No changes were made in the individual instruments configured in the workcell. Based on these, limited performance tests were conducted on the most complex workcell configuration (e.g., model DxH 2401). The performance studies were conducted at either the Beckman Coulter facility in Miami, Florida or at the London Health Sciences Centre, London, Ontario, Canada.

a. Accuracy:

Measurement Procedures Comparison: Whole Blood

The objective of the study was to verify that whole blood results on the DxH 800 v3.0 meet the bias specifications when compared to the DxH 800 v2.0 predicate. Trueness was established in accordance with CLSI H26-A2 and EP9-A3.

The study included 333 whole blood specimens distributed across the analytical measuring interval (AMI). Spent normal and clinical specimens from a comprehensive and diverse range of hematological conditions with hematological cellular characteristics at target ranges of the parameters to be tested were used. The specimens were tested in singlet on the DxH 800 v3.0 and the predicate DxH 800 v2.0 in the CBC/Diff and Reticulocyte (CDR) panel. A minimum of 100 specimens were tested on each DxH 800 v3.0 instrument in the workcell with the workstation software determining the specimen routing between instruments.

The regression approach described in CLSI EP9-A3 was used to estimate differences between the test DxH 800 v3.0 and the predicate DxH 800 v2.0 instruments.

Prior to statistical analysis, the data were inspected for outliers; no outliers were removed. Parameters flagged with R (Review Flag), or non-numeric results were excluded from analysis. Exclusions were made at the parameter level not the specimen level. There were no specimens excluded from the study.

Deming and Weighted Deming approaches were used to estimate the parameters of the regression model (slope, intercept, their 95% confidence intervals and correlation coefficient). Weighted Deming was used for counts, i.e., WBC, RBC, PLT, etc., since the scatter of the data (variability) was significantly related to the range of measurements (mean). The Deming approach was used for other parameters, except BA%. Passing and Bablok regression was used for BA% because the scatter of the data was not uniform throughout the range and a non-parametric approach was more appropriate. Bias between methods was calculated from the regression line at the 25th, 50th, and 75th percentile points of the range of the comparator and at medical decision points. Confidence limits of bias estimates were calculated based on standard errors of bias and 95% confidence. The upper/lower confidence limits were compared to the specifications.

The DxH 800 v3.0 is considered to be comparable to the DxH 800 v2.0 predicate if the upper/lower 95% confidence limit of the difference between the parameter results obtained from the data set for all other parameters is less than or equal to the acceptance limits defined. The DxH 800 v3.0 is considered to be comparable to the DxH 800 v2.0 predicate if the correlation coefficient for NRBC is greater than the specification.

All results met the acceptance criteria. The whole blood comparability results on the DxH 800 v3.0 demonstrated acceptable performance against the predicate DxH 800 v2.0.

Measurement Procedures Comparison: Body Fluid

The objective of the study was to verify that body fluid results on the DxH 800 v3.0 meet the bias specifications when compared to the predicate DxH 800 v2.0. Trueness was established in accordance with CLSI H26-A2 and EP9-A3.

The study included 110 specimens distributed across the AMI with spent body fluid specimens from a comprehensive and diverse range of hematological conditions whose body fluid characteristics satisfied the target ranges of the parameters to be tested. Body fluid specimen was spiked with spent whole blood and whole blood was diluted with normal saline; all samples were analyzed in the body fluid test mode. The specimens were comprised of a mixture of the body fluid types (e.g., CSF, synovial, and serous). The specimens were tested in duplicate on the DxH 800 v3.0 and the predicate DxH 800 v2.0 in the body fluids mode. The specimens were equally distributed across the three DxH 800 v3.0 instruments within the workcell.

Prior to statistical analysis, the data were inspected for outliers; no outliers were removed. Individual parameter results for specimens that were below the measuring range were excluded from analysis. There was one specimen excluded from the study.

Weighted Deming approaches were used to estimate the parameters of the regression model (slope, intercept, their 95% confidence intervals, and correlation) since the scatter of the data (variability) was significantly related to the range of measurements (mean). Bias between methods was calculated from the regression line at the 25th, 50th, and 75th percentile points of the range of the comparator. Confidence limits of bias estimates were calculated based on standard errors of bias and 95% confidence. The upper/lower confidence limits were compared to the specifications.

The DxH 800 v3.0 is considered to be comparable to the DxH 800 v2.0 predicate if the upper/lower 95% confidence limit of the difference between the parameter results is less than or equal to the acceptance limits defined.

All results met the acceptance criteria. The body fluid bias results on the DxH 800 v3.0 demonstrated acceptable performance against the predicate DxH 800 v2.0.

b. *Precision/Reproducibility:*

Imprecision (Repeatability): Whole Blood

The objective was to verify that the Whole Blood Imprecision (Repeatability) of the proposed DxH 800 system (v3.0) meets the performance specifications. Imprecision for Whole Blood was evaluated in accordance with CLSI H26-A2.

Specimens were collected to evaluate repeatability in the lower ranges for WBC, RBC, and PLT parameters. Where specimens could not be obtained through the collection of routine spent samples, specimens were manipulated to achieve the target parameter value prior to testing. At least 5 samples with 10 replicates for each sample were included in the analysis. Different samples were tested for different parameters. The specimens were randomly distributed across the three DxH 800 v3.0 instruments in the workcell. Exclusions were made at the parameter level not the specimen level. Parameter results for specimens having System Messages, System Status messages and “R” flags were excluded. No specimens were removed from analysis.

Calculations were performed separately for each parameter. ANOVA was used to partition sample-to-sample variability from the within sample variability. Test for homogeneity for each parameter confirmed the pooling of variances. Within sample variance component estimated the repeatability of the system. Upper 95% confidence limit of the repeatability variance was calculated using the chi-square distribution. CV% was calculated by dividing the square roots of variance and its upper limit with the average of all samples. Upper limit of the repeatability CV% was compared to the repeatability specification.

The whole blood imprecision (repeatability) results on the DxH 800 v3.0 demonstrated acceptable performance. All the results met the acceptance criteria. For all parameters, the upper 95% confidence limit was within the specification. The descriptive statistics, repeatability CV%, upper 95% confidence limits of the repeatability CV%, acceptance limits, and conclusions are presented below.

Repeatability Performance

Parameter	Number of Samples	Mean	CV%	95% Upper Limit (CV%)	Acceptance Limits (CV%)	Conclusion
WBC	6	0.22	4.24	5.08	15.0	Pass
RBC	5	1.69	0.74	0.90	5.0	Pass
PLT	6	6.79	12.41	14.77	20.0	Pass

Imprecision (Repeatability): Body Fluid

The objective was to verify that the Body Fluid Imprecision (Repeatability) of the proposed DxH 800 system (v3.0) meets the performance specifications. Imprecision for Body Fluid was evaluated in accordance with CLSI H26-A2.

Diluted whole blood specimens were prepared such that the BF-TNC and BF-RBC parameters were within the specified target ranges. At least 5 samples were included for each target range with 10 replicates tested in the body fluids mode from each sample. Different specimens were tested for the different parameters. The specimens were randomly distributed across the three DxH 800 v3.0 instruments in the workcell. No data was excluded from the analysis.

Calculations were performed separately for each parameter. ANOVA was used to partition sample-to-sample variability from the within sample variability. Test for homogeneity for each parameter confirmed the pooling of variances. Within sample variance component estimated the repeatability of the system Upper 95% confidence limit of the repeatability variance was calculated using the chi-square distribution. CV% was calculated by dividing the square roots of variance and its upper limit with the average of all samples. Upper limit of the repeatability CV% was compared to the repeatability specification.

The body fluids imprecision (repeatability) results on the DxH 800 v3.0 demonstrated acceptable performance. All the results met the acceptance criteria. For all parameters, the upper 95% confidence limit was within the specification. The descriptive statistics, repeatability CV%, upper 95% confidence limits of the repeatability CV%, acceptance limits, and conclusions are presented below.

Body Fluid Imprecision

Parameter	Number of Samples	Range	Mean	CV%	95% UpperLimit (CV%)	Acceptance Limits (CV%)	Conclusion
BF-TNC	5	20 to <50 cells/mm ³	29.85	9.74	11.81	25.0	Pass
BF-RBC	6	1,000 to <5,000 cells/mm ³	4086.37	4.49	5.34	20.0	Pass

c. Linearity:

Linearity: Whole Blood

The objective of the study was to verify that the Whole Blood Linearity of the proposed DxH 800 system (v3.0) meets the performance specifications. Linearity evaluated in accordance with CLSI EP06-A.

Linearity was assessed by demonstrating that the reported results are directly proportional to the concentration of the measurand in a test sample for WBC, RBC, HGB, and PLT parameters across the analytical measuring range. Testing assessed whole blood linearity using whole blood and cell control analog samples on the proposed DxH 800 system (v3.0).

Dilution series were prepared covering the analytical measuring interval for each

parameter. A mixture of whole blood and plasma were used for RBC and HGB and a mixture of cell control analogs and media were used for WBC and PLT to create the dilution series. To cover the entire parameter range using a single set of dilutions, the dilution schemes designed for WBC and PLT included more dilution points in the lower end of the range. This distribution allowed for higher resolution in the lower end of the range to capture medical decision points while covering the full range. Equally spaced dilutions were used for RBC and HGB since their ranges were relatively narrower and the medical decision levels were captured adequately. All dilutions were run in quadruplicate on each of the three DxH 800 instruments in the workcell.

Limits for Linearity (Specifications)

Parameter	Range	Limit
WBC	0.05 – 2.0 >2.0 – 100.0 >100.0 – 400.0	$r^2 > 0.95$ and ± 0.1 or $\pm 10\%$ ± 0.2 or $\pm 3\%$ $\pm 5\%$
RBC	0.005 – 8.50	$r^2 > 0.95$ and ± 0.05 or $\pm 2\%$
HGB	0.10 – 25.50	$r^2 > 0.95$ and ± 0.20 or $\pm 3\%$
PLT	3.0 – 3000.0	$r^2 > 0.95$ and ± 5.5 or $\pm 5\%$

The linearity data was analyzed independently for each DxH 800 instrument in the workcell. 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 the acceptance criteria.

Weighted least squares method was used to estimate the linear, quadratic and cubic regression parameters. The reason for choosing the weighted least squares method was the significant dependency of variability to the measuring range (heteroscedacity).

All analyses met r^2 acceptance criteria. The linearity results for WBC, RBC, HGB, and PLT on the DxH 800 v3.0 demonstrated acceptable linearity performance.

Linearity: Body Fluid

The objective of the study was to verify that the Body Fluid Linearity of the proposed DxH 800 system (v3.0) meets the performance specifications. Linearity was evaluated in accordance with CLSI EP06-A.

Linearity was assessed by demonstrating that the reported results are directly proportional to the concentration of the measurand in a test sample for body fluids for BF-RBC and BF-TNC parameters across the analytical measuring range. Testing assessed body fluid linearity using whole blood or cell control analogs on the proposed DxH 800 system (v3.0).

Dilution series of whole blood (BF-RBC) or cell control analogs (BF-TNC) were made to cover the analytical measuring interval of the body fluid parameter. To cover the entire parameter range a single set of 15 dilutions were made. All dilutions were run in quadruplicate on each of the three DxH 800 v3.0 instruments in the workcell.

Body Fluid Linearity Specifications

Parameter	Specifications
BF-RBC	$r^2 > 0.95$ and ± 500 or $\pm 5\%$ Bias
BF-TNC	$r^2 > 0.95$ and ± 5 or $\pm 10\%$ Bias

The linearity data was analyzed independently for each DxH 800 instrument in the workcell. Statistical evaluation of linearity followed CLSI EP06-A. 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 the acceptance criteria.

Weighted least squares method was used to estimate the linear, quadratic and cubic regression parameters. The reason for choosing the weighted least squares method was the significant dependency of variability to the measuring range (heteroscedacity).

All analyses met r^2 acceptance criteria. The results for BF-RBC and BF-TNC on the DxH 800 v3.0 demonstrated acceptable body fluids linearity performance.

d. Carryover:

The objective of the study was to verify that the Whole Blood Carryover of the proposed DxH 800 system (v3.0) meets the performance specifications. The study was performed in accordance with CLSI H26-A2.

Carryover was assessed by running whole blood specimens with high parameter values followed by DxH Diluent (diluent). Whole blood specimens were selected or altered to obtain the WBC, RBC, HGB, and PLT target values below. Each whole blood specimen was analyzed three times followed by diluent analyzed three times. A minimum of three carryover cycles (i.e., three different specimens) per parameter were tested on each DxH 800 instrument in the workcell.

Target Values

Parameter	Test Value
WBC	>90
RBC	>6.2
HGB	>22
PLT	>900

Carryover Specifications

Parameter	% Carryover
WBC	≤ 0.5%
RBC	≤ 0.5%
HGB	≤ 1.0%
PLT	≤ 1.0%
Parameter	Carryover (events or cells counted)
NRBC	≤ 75 events (WBC = 0.0 – 300.0)
DIFF	≤ 200 events
Retic	≤ 600 events

All results met the acceptance criteria. The whole blood carryover results for the DxH 800 v3.0 demonstrated acceptable performance.

Carryover: Body Fluids

The objective of the study was to verify that the Body Fluid Carryover of the proposed DxH 800 system (v3.0) meets the performance specifications. The study was performed in accordance with CLSI H26-A2.

Carryover was assessed by running whole blood specimens with high parameter values followed by DxH Diluent (diluent). Whole blood specimens were selected having WBC, and RBC values as listed below. Each whole blood specimen was analyzed three times in the CDR mode followed by diluent analyzed three times in the BF (body fluids) mode. A minimum of three carryover cycles (i.e., three different specimens) per parameter were tested on each DxH 800 instrument in the workcell.

Target Values

Parameter	Test Value
WBC	>90
RBC	>6.2

Carryover Specifications

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

The carryover for BF-TNC and BF-RBC parameters is reported as the total cells counted. The results are considered acceptable if the number of cells for each diluent is less than the specification.

All results met the acceptance criteria. The body fluid carryover results for the DxH 800 v3.0 demonstrated acceptable performance.

e. Interfering Substances:

Refer to 510(k) cleared device: k120771

2. Other Supportive Instrument Performance Data Not Covered Above:

a. Electromagnetic Compatibility/Interference:

The objective of the study was to verify that the electromagnetic compatibility (EMC) status of individual DxH 800 and DxH SMS instruments are not impacted when configured in a workcell configuration.

The required intrinsic immunity level to preclude EMC interference against emissions of nearby devices for the DxH 800 is 3 volts/meter. An assessment of the DxH 800's intrinsic level of immunity to preclude EMC interference against emissions of nearby devices was performed. Both the DxH 800 and DxH SMS have a maximum permissible emission limit of 0.0007 volts/meter. Testing of the individual devices showed acceptable performance to these limits. The required immunity level for both is 3 volts/meter. Therefore, the intrinsic level of RF immunity for both devices is orders of magnitude greater than the emission limit of each device. Based on these factors, it is unlikely that the EMC interference would be increased in a connected DxH workcell as compared to a stand-alone DxH 800.

b. Vibration Testing

The objective of the study was to determine the impact of vibration due to the coupling of multiple instruments in a workcell configuration on measurement results.

The impact of connecting DxH 800 and DxH SMS instruments in workcell configurations was assessed by comparing the System Backgrounds and AC RMS (alternating current root mean square) noise for each blood cell measurement channel against the specification limits. Measurement results will not be impacted if System Backgrounds and AC RMS noise remain within specification during vibration testing.

The testing protocol included: instrument Shutdown and Startup; completion of daily checks including System Backgrounds, and; for each instrument, capture 20 AC RMS noise measurements for each blood cell measurement channel of the CBC and VCSn modules, while all of the other instruments (DxH 800 and DxH SMS) in the test configuration were continuously running.

Eleven test cases were executed representing the different workcell configurations. All test cases for the Standalone and Connectivity Workcell configurations passed the AC RMS noise measurements as well as System Backgrounds. Based on this study, there is no evidence that the coupling of multiple instruments in a workcell configuration will have an impact on measurement of results.

c. Determination of Limit of Blank (LoB), Lower Limits of Detection (LLoD) and Quantitation (LLoQ):

The objective of the study was to verify that the LoB, LLoD and LLoQ of the DxH

800 v3.0 meet the performance specifications. The studies were designed based on CLSI H26-A2.

LoB, LoD, and LLoQ testing was performed for the parameters defined below. These are parameters where there is a clinical interest (medical decision level) on very low or near zero values.

- Whole blood – WBC and PLT
- Body Fluid – TNC and RBC

Limit of Blank

The test was conducted on each of the three DxH 800 v3.0 instruments in the workcell. On each test instrument, blank samples consisting of DxH Diluent (diluent) were tested over three days as follows:

- For the whole blood mode, testing of the diluent blanks was distributed over the different analysis modes where five diluent blanks were analyzed in each mode (CBC, CD, CDR and CR) for three days. This testing scheme resulted in 40 daily runs (20 AM, 20 PM) which then totaled 120 whole blood runs over the 3 day study.
- For the body fluids mode, testing of the diluent blanks resulted in 40 daily runs (20 AM, 20 PM) which then totaled 120 body fluid runs over the 3 day study.

A minimum of two reagent lots were used for the DxH Diluent and the DxH Cell Lyse installed on the DxH 800 Workcell instruments over the 3 day period.

The limits of blank (LoB) were calculated separately for 3 connected DxH 800 v3.0 instruments. The nonparametric approach based on 95% percentiles was used to calculate LoB for each instrument.

Lower Limit of Detection and Lower Limit of Quantitation

To test for LLoD and LLoQ, an individual set of dilutions on a sample was prepared to obtain a stock solution with a value in one of the specified target ranges. The concentration of the stock solution was verified on the DxH 800 v2.0 predicate instrument. Four samples per parameter were used for a total of 16 samples.

Dilution series were prepared of the stock solution in 10 percent increments from 0% to 100%. Three sets of dilutions were prepared; one set of dilutions was analyzed on each of the three DxH 800 v3.0 instruments. Five replicates of each dilution level were analyzed on each DxH 800 v3.0 instrument in the appropriate analytical mode, either CBC or BF. The analysis was repeated 24 hours later on each of the three DxH800 v3.0 instruments.

Bias was established using normal whole blood samples analyzed in duplicate in the CBC analytical mode on the DxH 800 v2.0 predicate instrument and each of the DxH

800 v3.0 instruments in the workcell. Five bloods were analyzed each day for 12 days for a total of 60 bloods.

There was a significant relationship between precision and concentration for each parameter. Consequently, the precision profile approach was used to estimate LLoD and LLoQ. LLoQ was calculated based on total error composed of the within laboratory variability component and bias component.

Estimated Bias

Parameter	Instrument	% Bias	Specifications
WBC	AU45701	1.30%	10%
	AU46728	2.29%	
	AU46737	1.88%	
PLT	AU45701	-1.70%	7%
	AU46728	0.36%	
	AU46737	-1.31%	
BF-TNC	AU45701	1.30%	10%
	AU46728	2.29%	
	AU46737	1.88%	
BF-RBC	AU45701	-0.38%	5%
	AU46728	-0.19%	
	AU46737	0.91%	

The Limit of Blank, Lower Limit of Detection and Lower Limit of Quantitation results on the DxH 800 v3.0 demonstrate acceptable performance. Summary results of the LoB, LLoD, LLoQ and upper confidence limits are shown below.

Summary results of LoB and upper confidence limits

Parameter	Instrument	LoB	Specifications	Conclusion
WBC	AU45701	0.010	0.02	Pass
	AU46728	0.010		
	AU46737	0.010		
PLT	AU45701	0.80	1.5	Pass
	AU46728	0.65		
	AU46737	0.65		
BF-TNC	AU45701	3	10	Pass
	AU46728	3		
	AU46737	2		
BF-RBC	AU45701	187	500	Pass
	AU46728	172		
	AU46737	381		

Summary results of LLoD and upper confidence limits

Parameter	Instrument	LLoD	Specifications	Conclusion
WBC	AU45701	0.015	0.03	Pass
	AU46728	0.015		
	AU46737	0.016		
PLT	AU45701	1.28	2.3	Pass
	AU46728	1.08		
	AU46737	0.98		
BF-TNC	AU45701	8	15	Pass

	AU46728	6		
	AU46737	8		
BF-RBC	AU45701	371	750	Pass
	AU46728	307		
	AU46737	647		

Summary results of LLoQ and upper confidence limits

Parameter	Instrument	LLoQ	Specifications	Conclusion
WBC	AU45701	0.016	0.05	Pass
	AU46728	0.018		
	AU46737	0.020		
PLT	AU45701	1.29	3	Pass
	AU46728	1.12		
	AU46737	1.28		
BF-TNC	AU45701	10	20	Pass
	AU46728	7		
	AU46737	12		
BF-RBC	AU45701	567	1000	Pass
	AU46728	421		
	AU46737	765		

d. DxH SMS Performance Test Strategy

The output of the DxH SMS is limited to the delivery of a physical slide. The device does not generate test results; it only produces a slide that is read on a separate device by a technician. Based on this, the DxH SMS test strategy was designed to evaluate the critical attributes of the slide output, specifically slide quality and carryover.

Testing was performed on the most complex workcell (model DxH 2401).

DxH SMS Slide Quality

The objective was to verify that the DxH SMS produces slides that meet the slide quality specifications. Slide quality was established in accordance with CLSI H20-A2.

Slides were prepared in duplicate for 104 specimens on the DxH SMS in the workcell. The slides were evaluated by two independent readers following the Requirements for an Acceptable Blood Film (section 6.3.1) described in CLSI H20-A2. Additionally, overall slide quality was assessed.

Acceptance Criteria: Slides must meet the Requirements for an Acceptable Blood Film (section 6.3.1) described in CLSI H20-A2:

1. Sufficient working area.
2. Minimum 2.5 cm in length terminating at least 1 cm from the end of the slide.
3. Gradual transition in thickness from the thick to the thin areas, ending in a feathered edge.

4. Acceptable morphology within the working area.
5. Narrower than the slide on which the film is spread, with smooth continuous side margins that are accessible for oil immersion examination.
6. No artifact introduced by the technique.
7. Minimum distributional distortion.
8. A far end that becomes gradually thinner, without grainy streaks, troughs, or ridges, all of which indicate an increased number of WBC carried into this area.

Additionally, >95% of the slides must be readable.

All results met the acceptance criteria. The DxH SMS produces slides that meet the slide quality specifications.

DxH SMS Carryover

The objective was to verify that the Carryover of the DxH SMS meets the performance specifications.

A series of slides from normal whole blood samples followed by control material containing analog cells were prepared by the DxH SMS in alternating order as described below.

- Three normal whole blood samples
- One control sample with a WBC value of $50 \times 10^3/\mu\text{L}$
- Three normal whole blood samples
- One control sample with a WBC value of $150 \times 10^3/\mu\text{L}$
- Four normal whole blood samples
- One control sample with a WBC value of $400 \times 10^3/\mu\text{L}$
- Three normal whole blood samples
- One control sample with a WBC value of $50 \times 10^3/\mu\text{L}$
- Three normal whole blood samples

The whole blood slides were assessed for carryover of control analog cells by performing a 400 cell differential on each slide using the Cellavision DM96 (k080595).

Slides must contain ≤ 1 analog cell in 400 WBCs in the working area of the slide. There were no analog cells observed on any of the whole blood slides. The DxH SMS carryover demonstrated acceptable performance.

An additional carryover study was conducted on the DxH SMS using whole blood samples with abnormal WBC types. It was designed to test for carryover of abnormal WBC cell types using the DxH SMS within a connected workcell. The carryover study was repeated 5 times using 5 different high target value (HTV) abnormal WBC specimens.

A low target value (LTV) sample free of abnormal WBC cells was identified with sufficient volume for each carryover study. Each sample was leukodepleted using CD45RO conjugated beads to reduce the background WBC and enhance the detection sensitivity of the carryover studies. Leukodepletion did not affect the other cell populations and some residual WBC may have remained.

For each carryover study, a set of seven slides (1 Background LTV, 3 HTV, 3 LTV) were prepared on the DxH SMS. The same specimen was used to prepare the Background LTV and the individual LTV slides. A manual differential was performed on the Background LTV slide, the third HTV slide and the first LTV slide. For the HTV samples, the manual differential was based on a 400 cell count. For LTV samples, due to the low cell concentration, all cells within the working area of the slide were read. A Cellavision DM96 was used to locate the events on the slide and the results were reviewed by a single operator.

The first LTV slide must contain ≤ 1 abnormal cell in the working area of the slide. There were no abnormal cells observed on any of the LTV slides from the five carryover studies.

All carryover studies met the acceptance criteria. The DxH SMS carryover demonstrated acceptable performance.

K. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

L. Conclusion:

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