510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
INSTRUMENT ONLY TEMPLATE

A. 510(k) Number:

k130253

B. Purpose for Submission:

New Device

C. Manufacturer and Instrument Name:

Beckman Coulter COULTER TQ-Prep Workstation
Beckman Coulter COULTER PrepPlus 2

D. Type of Test or Tests Performed:

Specimen Processors

E. System Descriptions:

1. Device Description:

COULTER PrepPlus 2

The COULTER PrepPlus 2 is an automated microprocessor-controlled pipetting and diluting system designed for automating sample preparation. It is capable of aspirating and dispensing whole blood samples, Beckman Coulter cleared flow cytometric IVD reagents and Flow-Count Fluorsphores. The PrepPlus 2 uses 12-tube specimen cassettes to hold patient samples. The PrepPlus 2 instrument can pierce the caps of specimen tubes and aliquot the specimens into daughter tubes.

COULTER TQ-Prep Workstation

The COULTER ImmunoPrep Reagent System is used with the COULTER TQ-Prep Workstation to prepare leukocytes from whole blood for measurements on cleared Beckman Coulter flow cytometers.

Prior to placement on the TQ-Prep Workstation, the user prepares the whole blood specimens according to the monoclonal antibody reagent IFU by adding the specified volume of specimen and monoclonal antibody reagent to 12 x 75 mm test tubes, vortex mixing, and incubating for the specified times (this can be done manually or with the PrepPlus2). Up to 32 samples containing the premixed sample of blood and antibody are presented to the TQ-Prep Workstation from a carousel capable of holding up to 32 test tubes. Then the TQ-Prep Workstation automatically adds, in this order:

- ImmunoPrep A Reagent – an erythrocytic lysing reagent which causes

simultaneous rapid destruction of the erythrocytes while leaving the leukocytes intact

- ImmunoPrep B Reagent – a leukocyte stabilizer which stops the action of the lysing reagent (ImmunoPrep A), and
- ImmunoPrep C Reagent – a cell membrane fixative which fixes the cell membranes preserving the form and structure of the leukocytes.

The TQ-Prep vortex mixes the sample with the addition of each reagent for specified times. Upon completion of specimen processing on the TQ-Prep Workstation, the samples are removed from the device and presented separately to a flow cytometer for analysis.

2. Principles of Operation:

COULTER PrepPlus 2

The PrepPlus 2 is a robotic module which has three functional axes: X/Y/Z. These axes are driven by stepper motors which are controlled by microprocessors mounted on printed circuit boards. The PrepPlus 2 is designed to move its sample probe tip to specific locations, detect liquid, and aspirate or dispense liquid. The PrepPlus 2 uses 12-tube specimen cassettes to hold patient samples. Only one orientation is permitted with respect to cassette introduction to the instrument. Orientation of the cassette on the device is controlled by the shape of the cassette and the receiving cradle and locking handle on the PrepPlus 2. It is physically impossible to seat the cassette onto the cradle in any orientation except the correct one. Specimen loading order on the device is identified by the numbers on the top of the cassette receiver as shown in the image below. The front side cassette orders tubes from 1-12 in a left to right orientation. The back side cassette orders tubes from 13-24 from right to left. There are two software programs that come with the PrepPlus 2:

- Operating System: This is loaded into the TQ-Prep Workstation when the PrepPlus 2 is installed. The user runs both the PrepPlus 2 and the TQ-Prep Workstation from the TQ-Prep Workstation touch screen commands.
- Panel Definition software: This is provided on 3½ in. disks. The user can load it into any computer that fits the requirements defined in the product labeling. This software allows user to define panels, reagent racks, and control/calibrator racks.

COULTER TQ-Prep Workstation

The TQ-Prep Workstation has a system microprocessor located on the Control Interface card controls the motors, sensors, syringes, the cover/lid interlock switches, reagent level sense probes and an internal communication link to the system microprocessor assembly.

The TQ-Prep Workstation PREP I system is partitioned into the following modules:

- MQP Module: consists of assemblies which include electronics and mechanisms to rotate the reaction carousel, to move the reaction tube under the reagent delivery head, to move the reagent delivery head to the delivery position, to dispense lyse, fixative and stabilizing reagent to the reaction tube, to mix the

reaction tube, and to remove reagent prime fluid to waste. The chassis and door consists of mechanical elements which provide structural support and protection for the instrument components. The covers and skins provide cosmetic value. The hardware user interface consists of a touch screen display.

- Software Module: consists of program instructions and data to control the operation of the MQP and User Interface modules.
- Reagents Module: consists of the current ImmunoPrep reagents lysing agent, fixative and stabilizing reagents and the Option reagent (distilled water).

3. Modes of Operation:

   Semi-Automated

4. Specimen Identification:

   Manual, controlled by operator.

5. Specimen Sampling and Handling:

   Specimens are whole blood specimens collected into approved tubes

6. Calibration:

   Not applicable.

7. Quality Control:

   The accuracy of the COULTER TQ-Prep and PrepPlus 2 Systems depend on the laboratory following the quality control instructions for Beckman Coulter cleared flow cytometric IVD reagents, the ImmunoPrep Reagent system in context of the Beckman Coulter flow cytometer system

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 § 862.2750, Pipetting and Diluting System for Clinical Use

2. Classification:

   Class I

3 Product code:

   PER, Automated pipetting, diluting and specimen processing workstations for flow cytometric analysis

4. Panel:

   Clinical Chemistry (75)

G. Intended Use:

1. Indication(s) for Use:

   COULTER TQ-Prep Workstation

   Intended Use:
   The COULTER TQ-Prep Workstation is intended to prepare leukocytes from whole blood for In Vitro Diagnostic (IVD) Use when used with the COULTER ImmunoPrep Reagent System and cleared Beckman Coulter IVD applications on cleared Beckman Coulter flow cytometers.

   Indications for Use:
   Pipetting of ImmunoPrep Reagent System (lyse, stabilizer, and fixative reagents) to samples prepared either manually or with the COULTER PrepPlus 2 sample preparation device to achieve lysis of whole blood samples. Use of COULTER TQPrep with cleared Beckman Coulter flow cytometers is described in each application's Instructions for Use. For In Vitro Diagnostic Use Only.

   COULTER PrepPlus 2

   Intended Use:
   The COULTER PrepPlus 2 when used in combination with the COULTER TQ-Prep Workstation, is intended to prepare human whole blood for In Vitro Diagnostic (IVD) Use with cleared Beckman Coulter IVD applications on cleared Beckman Coulter flow cytometers.

   Indications for Use:
   Pipetting blood, cleared Beckman Coulter IVD reagents and Flow-Count Fluorospheres to prepare samples for flow cytometric analysis. Use of PrepPlus 2 with cleared Beckman Coulter flow cytometers is described in each application's Instructions for Use. For In Vitro Diagnostic Use Only.

2. Special Conditions for Use Statement(s):

   For prescription use only.

H. Substantial Equivalence Information:

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

New Device	Predicate	Manufacturer	510(k) Number
TQ-Prep	Q-Prep	Beckman Coulter, Inc.	k874188
PrepPlus 2	Manual Pipette	Various	Not applicable

2. Comparison with Predicate Device:

COULTER TQ-Prep Workstation:

Similarities/Differences		
Item	New Device	Predicate
	COULTER TQ-Prep Workstation	Q-Prep (k874188)
Intended Use	The COULTER TQ-Prep Workstation, when used with the COULTER ImmunoPrep Reagent System, is intended to prepare leukocytes from whole blood for flow cytometric analysis on the Beckman Coulter flow cytometers as described in the Indications for Use. For In Vitro Diagnostic Use	Q-PREP is used to prepare leukocytes for immunofluorescence measurements on optical flow cytometers.
Manufacturer	Beckman Coulter, Inc.	Same
Controlling software	The system microprocessor (386) assembly controls the touch screen, disk drive, power indicator, beeping device, and an internal communication link to the Control Interface card. A microcontroller, located on the Control Interface card, controls the motors, sensors, syringes, the cover/lid interlock switches, reagent level sense probes and an internal communication link to the system microprocessor assembly.	The timing electronics are on a single circuit board. They control the syringe delivery order, individual syringe priming cycles, continuous mix cycle, cycle reagent addition and mixing, and stop cycle.
Lyse Reagents	ImmunoPrep A: Erythrocyte Lysing Reagent ImmunoPrep B: Stabilizing Reagent ImmunoPrep C: Cell Membrane Fixative	Same

Similarities/Differences		
Item	New Device	Predicate
	COULTER TQ-Prep Workstation	Q-Prep (k874188)
Lyse Reagent Volume Range	ImmunoPrep A: 0.600 mL ± 5 % ImmunoPrep B: 0.265 mL ± 5 % ImmunoPrep C: 0.100 mL ± 5 %	Same
Timing	Premix: 2 ± 1 sec Lysing: 8 ± 1 sec Stabilizing: 10 ± 1 sec Fixative: 10 ± 1 sec	Same
Syringe Type	Stepper Motor Tri-Continent Syringes	CAM-driven displacement syringes
Mixing	The tube lifter/vortex mixer uniformly first lifts the tube up into the dispensing head, then mixes reagents in the sample. The mixer rotates at 1400-1800 rpm.	The mixer has a rotating arm that turns the bottom of the 12 x 75 mm test tube while a clip holds the top of the test tube in a fixed position. A circular rubber grommet holds the test tube in the arm. The arm rotates at a rate of 1400 to 1800 rpm.
Sample Introduction	Automated presentation to sample processing area with Multi-tube Carousel Loader (MCL) from 32 test tube (12 x 75 mm) capacity carousel	Manual presentation into a tube location on front of instrument via tube access door. Single 12 x 75 mm tube only.
Sample Identification	Manual, controlled by operator.	Same
Quality Control Techniques	Gravimetric calibration	Same

COULTER PrepPlus 2:

Similarities/Differences		
Item	New Device	Predicate
	COULTER PrepPlus 2	Manual Pipette
Intended Use	The COULTER PrepPlus 2, when used in combination with the COULTER TQ-Prep, is intended to prepare human whole blood for flow cytometric analysis on Beckman Coulter flow cytometers as described in the Indications for Use. For In Vitro Diagnostic Use.	Delivery of a specified volume of liquid. In the tetraCHROME reagent application, it delivers whole blood, ImmunoTrol and ImmunoTrol Low Cells, tetraCHROME reagents, and Flow-Count Fluorospheres.

Similarities/Differences		
Item	New Device	Predicate
	COULTER PrepPlus 2	Manual Pipette
Manufacturer	Beckman Coulter, Inc.	Various
Controlling software	Operating System – Loaded into the COULTER TQ-Prep Workstation. The user runs both the PrepPlus 2 and the TQ-Prep Workstation from the TQ-Prep Workstation touch screen commands. Panel Definition software – This software allows the definition of panels, reagent racks, and control/calibrator racks. Stand alone Panel Definition software also available.	Not applicable
Sample Identification	Manual, controlled by operator.	Same
Sample Introduction	Automated presentation with Multi-tube Carousel Loader (MCL) from 32 test tube (12 x 75 mm) capacity carousel	Manual presentation.
Sample Contact Material	Teflon-coated sample probe	Polypropylene disposable tip
Cleaning Cycle Between Samples	Executed with IsoFlow Sheath Fluid in wash station after each liquid-handling function. Once daily COULTER CLENZ cleaning agent cleans and rinses the sample probe to prevent protein build-up.	Pipette tip replaced between samples
Volume Range	5 µL to 1,000 µL. (Volumes over 500 µL are delivered in multiple aliquots. Maximum aliquot volume is 500 µL.)	Manual, controlled by operator.
Syringe Size	1.0 mL	Not applicable
Specimen Tube Size	Based on the specimen tube's diameter: • 13-mm specimen cassette • 16-mm specimen cassette With Adaptor: • 75 mm specimen tubes • 2 mL specimen tubes (with 2 mL tube adaptor)	Variable

Similarities/Differences		
Item	New Device	Predicate
	COULTER PrepPlus 2	Manual Pipette
	• 3 mL specimen tubes (with 3 mL tube adaptor) • IMMUNO-TROL control tubes	
Specimen Cassette Sizes	12 specimens per cassette for 13-mm and 16-mm specimen tubes	Not applicable
Prepared Sample Tubes (Daughter Tubes)	12 x 75 mm straight polypropylene test tube, round bottom.	Same

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

CLSI EP-5A: Evaluation of Precision Performance of Clinical Chemistry.

CLSI EP-9A2: Method Comparison and Bias Estimation Using Patient Samples.

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

J. Performance Characteristics*:*

1. Analytical Performance:

a. Accuracy:

Accuracy was assessed based on Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline, CLSI document EP9-A2. Two Method Comparison studies were performed:

1. TQ-Prep (new device/test method) vs. Q-Prep (comparator/reference method) using manual sample pipetting and preparation
2. PrepPlus 2 and TQ-Prep (new device/test) vs. Manual Pipette and Q-Prep (comparator/reference method).

Each study used the CYTO-STAT® tetraCHROME™ reagents (CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 and CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5), Flow-Count Fluorospheres and the FC 500 Flow Cytometer with tetraCXP software.

One hundred thirty (130) specimens were divided into three clinical sites (1 internal and 2 external). Each site analyzed 43 or 44 specimens. Specimens were collected from patients presenting for diagnosis and /or prognosis of HIV or immune dysfunction between the ages of 18-85 years. For this population, the medical decision points for CD3+CD4+ absolute counts were of interest. The same specimens prepared manually and lysed using a Q-Prep workstation were compared to the same specimens prepared manually and automated using a PrepPlus2 unit and lysed using a TQ-Prep workstation. ImmunoPrep reagents were used on both lytic

workstations.

For CD3+/CD4+, CD3+/CD8+, CD3-/CD56+, CD19+ (percent and absolute values), and Total CD3+ upper 95% confidence limits of the bias for the combined dataset (n=130) were compared to the manufacture's defined accuracy specifications. Data meet specifications if the mean bias for absolute counts is ±40 cells/µL for ≤300 cells or ±13% for >300 cells and the mean bias for percent is ±1.5% for ≤40% or ±2.5% for >40%. Additionally, regression statistics were calculated by test site. Results for all individual sites showed a high correlation coefficient. The confidence intervals of the slopes and/or intercepts for all individual sites overlapped with the intervals of the same regression statistics of the combined data set. Regression analyses of the combined site results are summarized below:

tetraCHROME CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Reagent		Total CD3+		CD3+CD4+		CD3+CD8+	
Units		cells/µL	%	cells/µL	%	cells/µL	%
N		130		130		130	
Correlation		0.986	0.993	0.987	0.998	0.988	0.997
Mean	Manual Pipette vs. Q-Prep	1058	76.26	311	24.66	712	49.22
	Manual Pipette vs. TQ-Prep	1054	75.94	309	24.65	712	49.00
Slope		0.998	1.022	0.995	1.001	0.998	1.012
95%CI	Lower limit	0.976	0.997	0.972	0.985	0.978	1.00
	Upper limit	1.019	1.048	1.019	1.016	1.017	1.024
Intercept		-5.669	-2.032	0.285	-0.024	-3.072	-0.794
95%CI	Lower limit	-11.541	-4.031	-1.688	-0.349	-5.040	-1.405
	Upper limit	0.204	-0.032	2.258	0.301	-1.103	-0.184

tetraCHROME CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Reagent		Total CD3+		CD3-CD56+		CD19+	
Units		cells/µL	%	cells/µL	%	cells/µL	%
N		130		130		130	
Correlation		0.992	0.995	0.993	0.995	0.989	0.997
Mean	Manual Pipette vs. Q-Prep	1102	76.24	123	9.29	166	11.36
	Manual Pipette vs. TQ-Prep	1080	76.03	122	9.36	164	11.35
Slope		0.979	1.014	0.983	0.995	0.975	0.998
95%CI	Lower limit	0.964	0.996	0.959	0.970	0.955	0.982
	Upper limit	0.993	1.032	1.006	1.020	0.996	1.013
Intercept		-3.108	-1.268	-0.118	0.115	0.153	0.011
95%CI	Lower limit	-7.908	-2.649	-0.690	-0.100	-0.377	-0.125
	Upper limit	1.692	0.113	0.456	0.330	0.682	0.148

The PrepPlus 2 automated pipetting method used with the TQ-Prep workstation lytic system demonstrated equivalent performance to the manual pipetting method and Q-Prep lytic system using tetraCHROME reagents and FlowCount to enumerate the absolute count directly. The following two tables summarize combined site regression analysis results:

tetraCHROME CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Reagent		Total CD3+		CD3+CD4+		CD3+CD8+	
Units		cells/µL	%	cells/µL	%	cells/µL	%
N		130		130		130	
Correlation		0.981	0.994	0.990	0.997	0.983	0.998
Mean	Manual Pipette vs. Q-Prep	1058	76.26	311	24.66	712	49.22
	PrepPlus1/TQ-Prep	1129	76.08	325	24.50	768	49.27
Slope		1.072	1.029	1.041	1.000	1.067	1.014
95%CI	Lower limit	1.049	1.004	1.019	0.980	1.045	1.002
	Upper limit	1.096	1.053	1.064	1.021	1.090	1.027
Intercept		-9.812	-20361	1.929	-0.169	-2.204	-0.659
95%CI	Lower limit	-16.321	-4.284	-0.316	-0.593	-5.551	-1.256
	Upper limit	-3.304	-0.439	4.174	0.256	1.143	-0.062

tetraCHROME CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Reagent		Total CD3+		CD3-CD56+		CD19+	
Units		cells/µL	%	cells/µL	%	cells/µL	%
N		130		130		130	
Correlation		0.984	0.995	0.988	0.994	0.987	0.997
Mean	Manual Pipette vs. Q-Prep	1102	76.24	123	9.29	166	11.36
	PrepPlus1/TQ-Prep	1114	76.14	126	9.41	169	11.34
Slope		1.011	1.021	1.016	1.003	1.001	1.013
95%CI	Lower limit	0.989	1.000	0.980	0.983	0.976	0.998
	Upper limit	1.034	1.042	1.051	1.024	1.026	1.028
Intercept		-3.932	-1.681	0.339	0.089	0.146	-0.166
95%CI	Lower limit	-11.260	-3.327	-1.065	-0.083	-0.401	-0.305
	Upper limit	3.396	-0.035	1.743	0.260	0.694	-0.028

b. Precision/Reproducibility:

A precision study was conducted according to CLSI EP5-A2, Evaluations of Precision Performance of Quantitative Measurement Methods. Two levels of control materials (IMMUNO-TROLCells and IMMUNO-TROL Low Cells) and Flow-Count Fluorospheres were evaluated in this study. The IMMUNO-TROL and IMMUNO-TROL Low control cells were prepared 2 times per day, with at least a two-hour interval, stained with CYTO-STAT tetraCHROME reagents CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 and CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5, respectively, and acquired twice on a FC 500 flow cytometer, for a total of 23 days for a total of 276 measurements. Three complete systems comprised of a TQ-Prep, PrepPlus 2, and FC 500 flow cytometer with tetraCXP software were tested. Within-run, between-run, between-days, between-instrument and total reproducibility were calculated. Measurements for this study were the absolute counts and percentages of the following lymphocyte subsets: CD3+, CD3+CD4+, CD3+CD8+, CD3-CD56+, CD19+. The manufacturer's acceptance criteria were as follows:

Analyte/Units of Measure	Total $CD3^+$% $CD3^+$ $CD4^+$% $CD3^+$ $CD8^+$% $CD3^-$ $CD56^+$% $CD19^+$ $CD4^+$%		Total $CD3^+$, cells/μL $CD3^+$ $CD4^+$, cells/μL $CD3^+$ $CD8^+$, cells/μL $CD3^-$ $CD56^+$, cells/μL $CD19^+$ $CD4^+$, cells/μL	
Mean	≤20%	>20%	<300 cells/ μL	≥300 cells/ μL
Repeatability Specification (%CV)	≤10%	≤5%	≤10%	≤5%
Reproducibility Specification (%CV)	≤15%	≤10%	≤15%	≤10%

Study results indicate that the device system performed according to the manufacturer's acceptance criteria.

A gravimetric study was also performed to evaluate the accuracy and precision of the fluid handling elements in the TQ-Prep and PrepPlus 2 sample preparation devices. Three of each instrument were tested by dispensing at least 20 replicates of each of their respective fluids. The results were analyzed for precision of the specified dispensed volumes against their respective specifications. The gravimetric studies demonstrated that the TQ-Prep and PrepPlus 2 performance for pipetting patient samples, controls, and reagents was found to be within the manufacture's specifications that the TQ-Prep and PrepPlus 2 perform with adequate accuracy and precision for delivering patient samples, controls, and reagents.

c. Linearity:

Not applicable

d. Carryover:

Specimen and Reagent Carryover were carried out to test both the carryover of cells and antibody reagents. Carryover was assessed based on recommendations contained in CLSI Document: *H26-A2, Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard -- Second Edition*. The studies were performed on three systems (each system composed of the TQ-Prep, PrepPlus 2 and FC 500 with textraCXP software) by running three high concentration samples analyzed consecutively three times (HTv1, HTv2, HTv3) followed immediately by testing a low concentration sample three times (LTv1, LTv2, LTv3). This run was repeated three times on each of the three systems, for both the specimen and reagent carryover studies. The percent carryover for specimen and reagent is calculated for absolute cell counts by formula referenced in H26-A2 (%Carryover = ((LTv1-LTv3)/(HTv3-LTv3))x100). These studies indicated that the complete systems, composed of the TQ-Prep, PrepPlus 2, and FC 500 with tetraCXP software,

performed within the manufactures specification that scatter and fluorescence carryover shall be <1% from one specimen to another in absolute number of counted cells.

e. Interfering Substances:

Not applicable

2. Other Supportive Instrument Performance Data Not Covered Above:

Not applicable

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.