



Food and Drug Administration
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December 17, 2015

BECTON, DICKINSON AND COMPANY
CATHERINE BESSETTE, PHD
SR. REGULATORY AFFAIRS SPECIALIST
2350 QUME DRIVE
SAN JOSE CA 95131

Re: K150815

Trade/Device Name: BD FACSPresto System
BD FACSPresto CD4/Hb Cartridge
BD FACSPresto CD4/Hb Cartridge Kit
BD Multi-Check Control
BD Multi-Check CD4 Low Control
Eurotrol FACSPresto Hb Control (Levels1-3)

Regulation Number: 21 CFR 864.5220

Regulation Name: Automated Differential Cell Counter

Regulatory Class: II

Product Code: PMG, OYE, GKL, JPK

Dated: November 18, 2015

Received: November 19, 2015

Dear Dr. Bessette:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)
K150815

Device Name

BD FACSPresto System
BD FACSPresto CD4/Hb Cartridge
BD FACSPresto CD4/Hb Cartridge Kit

Indications for Use (Describe)

BD FACSPresto System:

The BD FACSPresto System is an automated multicolor fluorescent imaging cytometer and absorbance spectrometer to be used in conjunction with single use reagent cartridges in performing the direct cell enumeration and measurement of absorbance spectrums.

- For use with the BD FACSPresto™ CD4/Hb Cartridge and BD FACSPresto™ CD4/Hb Cartridge Kit in the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings.
- For use in children, adolescents, and adults.
- For use with human whole blood from fingerstick and/or venous collections in K2 EDTA or K3 EDTA blood collection tubes.
- Not for point-of-care use.
- For in vitro diagnostic use.

BD FACSPresto CD4/Hb Cartridge & BD FACSPresto CD4/Hb Cartridge Kit:

The BD FACSPresto CD4/Hb Cartridge is a single use reagent cartridge to be used with the BD FACSPresto™ System for performing the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings.

- For use in children, adolescents, and adults
- For use with human whole blood from fingerstick and/or venous collections in K2 EDTA or K3 EDTA blood collection tubes.
- Not for point-of-care use.
- For in vitro diagnostic use.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

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Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

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Indications for Use

510(k) Number (if known)
K150815

Device Name
BD Multi-Check Control
BD Multi-Check CD4 Low Control

Indications for Use (Describe)

BD Multi-Check Control:

The BD™ Multi-Check control is intended as a complete process control for immunophenotyping by flow cytometry. It is a control for antibody staining, red blood cell (RBC) lysis, instrument setup and performance, and data analysis.

The BD™ Multi-Check control is also intended as a CD4 and %CD4 process control for antibody staining, instrument performance, and data analysis on the BD FACSPresto™ system, an imaging cytometer.

BD Multi-Check CD4 Low Control:

The BD™ Multi-Check CD4 low control is intended as a complete process control for immunophenotyping by flow cytometry. It is a control for antibody staining, red blood cell (RBC) lysis, instrument setup and performance, and data analysis.

The BD™ Multi-Check CD4 low control is also intended as a CD4 and %CD4 process control for antibody staining, instrument performance, and data analysis on the BD FACSPresto™ system, an imaging cytometer.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

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Indications for Use

510(k) Number (if known)

K150815

Device Name

Eurotrol FACSPresto Hb Control

Indications for Use (Describe)

Eurotrol FACSPresto Hb Control is an assayed hemoglobin control intended for in vitro diagnostic use in the verification of the precision and accuracy of the BD FACSPresto™ System.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Section 5 510(k) Summary

This 510(k) summary is being submitted in accordance with the requirements of Safe Medical Devices Act of 1990 and 21 CFR 807.92.

Date of Summary: November 13, 2015

5.1 Submitted By

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5.2 Trade Name/Device Name

Device Name: BD FACSPresto™ System
BD FACSPresto™ CD4/Hb Cartridge
BD FACSPresto™ CD4/Hb Cartridge Kit

Classification: Class II

Regulation Description: Automated Differential Cell Counter

Regulation Medical Specialty: Hematology

Product Code: PMG

Regulation: 21 CFR 864.5220

Device Name: BD Multi-Check Control
BD Multi-Check CD4 Low Control

Classification: Class II

Regulation Description: Hematology Quality Control Mixture

Regulation Medical Specialty: Hematology

Product Code: JPK

Regulation: 21 CFR 864.8625

Device Name: Eurotrol FACSPresto Hb Control (Levels 1-3)

Classification: Class II

Regulation Description: Hematology Quality Control Mixture

Regulation Medical Specialty: Hematology

Product Code: JPK

Regulation: 21 CFR 864.8625

5.3 Predicate Device

- BD FACSCalibur™ using BD Tritest CD3/CD4/CD45 with BD Trucount Tubes and BD MultiSet Software (K071141)
- R&D Systems' Whole Blood Flow Control, also known as StatusFlow (K961610 & BK990005)
- StatusFlow^{Lo} (K982231)
- Eurotrol Hb 301 Control (Levels 1-3) (BK030067)

5.4 Reference Device – Sysmex System

Sysmex™ Automated Hematology Analyzer KX-21N (K981761)

5.5 Predicate Device and Reference Device Selection Rationale

The FACSCalibur using BD Tritest CD3/CD4/CD45 with BD Trucount Tubes (K071141) was chosen as a predicate since it directly enumerates CD4 and %CD4 on the same specimen types. It is also used to characterize and monitor HIV-infected individuals.

The Sysmex Automated Hematology Analyzer KX-21N (K981761) was chosen as the reference device since it determines hemoglobin concentration on the same specimen type.

StatusFlow and StatusFlow^{Lo} were chosen as a predicate since they are the same reagent composition as the BD branded version of this product, known as BD Multi-Check Control and CD4 Low Control.

Eurotrol Hb 301 Control (Levels 1-3) was chosen as the predicate since they are the same reagent composition as the BD branded version of this product, known as Eurotrol FACSPresto Hb Control (Levels 1-3).

5.6 Basic Description of the Device

The BD FACSPresto System is an accurate, robust, and portable CD4, %CD4, and hemoglobin (Hb) System. The BD FACSPresto System has fluorescence microscopy and light absorbance capabilities. In addition, the instrument has integrated BD FACSPresto Software and instrument quality controls.

The BD FACSPresto CD4/Hb Cartridge contains antibody-fluorophore conjugates dried on a reagent disc and is embedded with reagent quality controls. The cartridge is designed with onboard reagents that mix well into the blood sample, and enumerate cells populations using fluorescence only. The cartridge is designed with fluidic properties that distribute a sufficient volume and sample into the imaging field of view for precise cell counting.

The BD FACSPresto CD4 and %CD4 assays are designed to stain cells with antibody-fluorophore conjugates for three color fluorescence reading using the BD FACSPresto System. CD4 PE-Cy5 stains CD4-positive cells; while CD3-

APC and CD45RA-APC stains total lymphocytes for use in the %CD4 calculation (CD3 stains T cells, while CD45RA stains B and NK cells in a patented formulation). CD14-PE is used for staining monocytes to exclude CD4 and/or CD45RA expressing monocytes from analysis.

BD Multi-Check Control and BD Multi-Check CD4 Low Control are process controls for the CD4 and %CD4 assay on the BD FACSPresto system. They are composed of human leukocytes and erythrocytes in a stabilizing medium and are intended to be used as a complete process control for antibody staining, instrument performance, and data analysis on the BD FACSPresto system.

The BD FACSPresto Hb assay is performed by a spectrophotometric method, using absorbance at an isobestic point for multiple forms of hemoglobin, with correction for scatter. The cartridge microfluidic channel permits absorbance reading of blood and of a reference area.

Eurotrol FACSPresto Hb Control is used as a process control for the Hb assay on the BD FACSPresto system. It is composed of purified bovine hemolysate and is intended to be used as an assayed hemoglobin process control intended for in vitro diagnostic use in the verification of the precision and accuracy of the BD FACSPresto System.

5.7 Indications for Use

BD FACSPresto System

BD FACSPresto System is an automated multicolor fluorescent imaging cytometer and absorbance spectrometer to be used in conjunction with single use reagent cartridges in performing the direct cell enumeration and measurement of absorbance spectrums.

- For use with the BD FACSPresto™ CD4/Hb Cartridge and BD FACSPresto™ CD4/Hb Cartridge Kit in the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings.
- For use in children, adolescents, and adults.
- For use with human whole blood from fingerstick and/or venous collections in K₂ EDTA or K₃ EDTA blood collection tubes.
- Not for point-of-care use.
- For in vitro diagnostic use.

BD FACSPresto CD4/Hb Cartridge

The BD FACSPresto CD4/Hb Cartridge is a single use reagent cartridge to be used with the BD FACSPresto™ System for performing the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and

determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings.

- For use in children, adolescents, and adults.
- For use with human whole blood from fingerstick and/or venous collections in K₂ EDTA or K₃ EDTA blood collection tubes.
- Not for point-of-care use.
- For in vitro diagnostic use.

BD Multi-Check Control

The BD™ Multi-Check control is intended as a complete process control for immunophenotyping by flow cytometry. It is a control for antibody staining, red blood cell (RBC) lysis, instrument setup and performance, and data analysis.

The BD™ Multi-Check control is also intended as a CD4 and %CD4 process control for antibody staining, instrument performance, and data analysis on the BD FACSPresto™ system, an imaging cytometer.

BD Multi-Check CD4 Low Control

The BD™ Multi-Check CD4 low control is intended as a complete process control for immunophenotyping by flow cytometry. It is a control for antibody staining, red blood cell (RBC) lysis, instrument setup and performance, and data analysis.

The BD™ Multi-Check CD4 low control is also intended as a CD4 and %CD4 process control for antibody staining, instrument performance, and data analysis on the BD FACSPresto™ system, an imaging cytometer.

Eurotrol FACSPresto Hb Control

Eurotrol FACSPresto Hb Control is an assayed hemoglobin control intended for in vitro diagnostic use in the verification of the precision and accuracy of the FACSPresto System.

The Indications for Use statements are similar to the predicate and reference devices. The differences do not affect the safety and effectiveness of the device relative to the predicate and reference devices.

5.8 Comparison to the Predicate and Reference Devices

Similarities/differences tables are provided for the BD FACSPresto system as compared to the BD FACSCalibur system (**Table 5-1**) and as compared to the Sysmex system (**Table 5-2**).

Regarding assay methodology, the BD FACSCalibur system utilizes cytometry through flow, while the BD FACSPresto utilizes cytometry through imaging. Although slightly different technologies, both designs function based on the same

principles. Both assay methods use fluorescently labeled antibodies to specifically label cell populations to classify them into sub-populations used for determining lymphocytes/ μL and CD4 lymphocytes/ μL . In each case, the sample is illuminated with light that excites the fluorescent labels and emitted light passes through optical filters to measure fluorescence intensity for each cell event.

Like flow cytometry, image cytometry is an event threshold or event based method. In both methods, fluorescence intensity is used to determine whether an object is there or not. The distinguishing features between flow and imaging cytometry are merely that (1) in flow, the sample is flowed in front of the detection system in a narrow fluid stream, while in imaging, the sample is static and spread out over the imaging field of view; and (2) flow cytometry includes light scatter intensity as an additional optical parameter. In either case, analysis algorithms are used to convert information about light intensities in different optical channels into cell ‘events’ and then further classify those events into cell populations of interest such as CD4 positive or negative lymphocytes.

Thus imaging cytometry, similar to flow cytometry, can be defined as the process of extracting and making sense of cytometric data obtained primarily from fluorescence signal intensities of cells specifically labeled with fluorescent antibodies.

Table 5-1: Similarities/Differences – Predicate Device (BD FACSCalibur system using Tritest) against Subject Device (BD FACSPresto System) for Absolute CD4 Count and %CD4 Assays.

Feature/ Attribute	BD FACSCalibur using BD Tritest CD3/CD4/ CD45 with BD Trucount Tubes (Predicate Device, K071141)	BD FACSPresto System for use with BD FACSPresto CD4/Hb Cartridge and BD FACSPresto CD4/Hb Cartridge Kit (Subject Device)
Intended Use/ Indications for Use	<ul style="list-style-type: none"> • For use with any flow cytometer equipped with a 488 nm laser and capable of detection in the ranges: 510-545 nm, 562-607 nm, and >650 nm • For use in erythrocyte-lysed whole peripheral blood • For use with or without isotype control • To characterize and monitor some forms of autoimmune disease • To characterize and monitor some forms of immunodeficiency disease, such as in HIV-infected individuals 	<p>BD FACSPresto System is an automated multicolor fluorescent imaging cytometer and absorbance spectrometer to be used in conjunction with single use reagent cartridges in performing the direct cell enumeration and measurement of absorbance spectrums.</p> <ul style="list-style-type: none"> • For use with the BD FACSPresto™ CD4/Hb Cartridge and BD FACSPresto™ CD4/Hb Cartridge Kit in the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings. • For use in children, adolescents, and adults. • For use with human whole blood from fingerstick and/or venous collections in K₂ EDTA or K₃ EDTA blood collection

Feature/ Attribute	BD FACSCalibur using BD Tritest CD3/CD4/ CD45 with BD Trucount Tubes (Predicate Device, K071141)	BD FACSPresto System for use with BD FACSPresto CD4/Hb Cartridge and BD FACSPresto CD4/Hb Cartridge Kit (Subject Device)
		<p>tubes.</p> <ul style="list-style-type: none"> • Not for point-of-care use. • For in vitro diagnostic use. <p>The BD FACSPresto CD4/Hb Cartridge is a single use reagent cartridge to be used with the BD FACSPresto™ System for performing the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings.</p> <ul style="list-style-type: none"> • For use in children, adolescents, and adults. • For use with human whole blood from fingerstick and/or venous collections in K₂ EDTA or K₃ EDTA blood collection tubes. • Not for point-of-care use. • For in vitro diagnostic use.
Device Classification and Product Code	Differential Cell Counter • Regulation Number: 21 CFR 864.5220 • Product Code: GKZ	Automated Differential Cell Counter • Regulation Number: 21 CFR 864.5220 • Product Code: PMG
Assay Methodology	Cytometry (flow)	Cytometry (imaging)
Assay Menu (FDA Cleared Assays)	Absolute CD4 count %CD4	Same
Results Reporting	<ul style="list-style-type: none"> • Absolute CD4 count (cells/uL) • %CD4 (the percentage of CD4 positive lymphocytes counted within the total lymphocyte population count) 	Same
Sample Type	Whole blood	Same
Sample Volume	Minimum 100 uL whole blood	1-2 drops venous or capillary whole blood
Sample Preparation	Manual pipetting for the lyse/wash or lyse/no-wash methods, or automated with the BD FACS Sample Prep Assistant (SPA) for the lyse/no-wash method	Manual introduction of venous or capillary blood onto BD FACSPresto Cartridge
Sample Analysis	• A controlled quantity of fluorescent beads is included in the sample through preparation in BD TruCount tubes to	• Capillary chamber height is precisely measured in manufacturing for each cartridge and encoded in the cartridge barcode. The size of the analysis image

Feature/ Attribute	BD FACSCalibur using BD Tritest CD3/CD4/ CD45 with BD Trucount Tubes (Predicate Device, K071141)	BD FACSPresto System for use with BD FACSPresto CD4/Hb Cartridge and BD FACSPresto CD4/Hb Cartridge Kit (Subject Device)
	<p>determine the volume of sample analyzed.</p> <ul style="list-style-type: none"> • Fluorescence intensity of beads and of cells of interest labeled by specific fluorescent antibodies is quantitatively measured. • Cells and fluorescent beads are algorithmically classified based on these signal intensities. • The number of cells in each classification and the volume of sample analyzed are used to calculate the reported assay results. 	<p>areas is determined by the instrument. The two are used to calculate the volume of analyzed sample.</p> <ul style="list-style-type: none"> • Fluorescence intensity of cells of interest labeled by specific fluorescent antibodies is quantitatively measured. • Cells are algorithmically classified based on these signal intensities. • The number of cells in each classification and the volume of sample analyzed are used to calculate the reported assay results.
Assay Principles	<p>CD4 and %CD4 flow cytometry assays using a 3 color direct immunofluorescent reagent to identify cell subset populations in lysed blood with automated analysis. Trucount beads are used for volume determination.</p>	<p>CD4 and %CD4 imaging cytometry assays using a 3-color direct immunofluorescent reagent to identify cell subset populations in whole blood with automated analysis. Precise dimensions of microfluidic channel and image area are used for volumetric determination.</p>
Optics Principles - CD4 and %CD4	<p>Fluorescence excitation of stained cells in flow stream by laser illumination; Fluorescence emission measured by PMTs</p>	<p>Fluorescence excitation of stained cells in microfluidic channel by LED illumination; Fluorescence emission measured by CCD camera imaging</p>
Fluidics	<p>Consists of a pinch valve assembly which controls the flow of sample, saline sheath fluid, and waste fluids during data acquisition.</p>	<p>Cartridge contains a microfluidic channel through which the sample fills by capillary action. After filling completes, sample is static during data acquisition.</p>
Instrument Setup and Quality Control	<p>Setup: Semi-automated setup using BD FACSComp software with BD Calibrite beads for setting PMT voltages, fluorescence compensation, and checking instrument sensitivity.</p>	<p>Setup: Automated instrument setup. Instrument QC: automated verification of instrument performance at power-on-self-test (POST) and during cartridge runs. Cartridge QC: rat anti-mouse antibodies bound to polystyrene beads confirm presence of sample and reagent.</p>
Software	<p>Integrated software on instrument and BD MultiSet Software on external computer</p>	<p>Integrated BD FACSPresto Software</p>

Table 5-2: Similarities/Differences –Reference (Sysmex Automated Hematology Analyzer KX-21N) against Subject Device (BD FACSPresto System) for total Hb assay.

Feature/ Attribute	Sysmex Automated Hematology Analyzer KX-21N (Reference Device, K981761)	BD FACSPresto System for use with BD FACSPresto CD4/Hb Cartridge and BD FACSPresto CD4/Hb Cartridge Kit (Subject Device)
Intended Use/ Indications for Use	The intended use of the Sysmex KX-21 is as an automated cell counter for in vitro diagnostic use in clinical laboratories.	<p>BD FACSPresto System is an automated multicolor fluorescent imaging cytometer and absorbance spectrometer to be used in conjunction with single use reagent cartridges in performing the direct cell enumeration and measurement of absorbance spectrums.</p> <ul style="list-style-type: none"> • For use with the BD FACSPresto™ CD4/Hb Cartridge and BD FACSPresto™ CD4/Hb Cartridge Kit in the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings. • For use in children, adolescents, and adults. • For use with human whole blood from fingerstick and/or venous collections in K₂ EDTA or K₃ EDTA blood collection tubes. • Not for point-of-care use. • For in vitro diagnostic use. <p>The BD FACSPresto CD4/Hb Cartridge is a single use reagent cartridge to be used with the BD FACSPresto™ System for performing the direct quantification and enumeration of CD4 absolute count, CD4 percentage of lymphocytes, and determination of hemoglobin concentration in normal and HIV positive patients, in conjunction with other laboratory and clinical findings.</p> <ul style="list-style-type: none"> • For use in children, adolescents, and adults. • For use with human whole blood from fingerstick and/or venous collections in K₂ EDTA or K₃ EDTA blood collection tubes. • Not for point-of-care use. • For in vitro diagnostic use.

Feature/ Attribute	Sysmex Automated Hematology Analyzer KX-21N (Reference Device, K981761)	BD FACSPresto System for use with BD FACSPresto CD4/Hb Cartridge and BD FACSPresto CD4/Hb Cartridge Kit (Subject Device)
Device Classification and Product Code	Automated Cell Counter (Particle Counter) • Regulation Number: 21 FR 864.5200 • Product Code: GKL and GKZ	Automated Differential Cell Counter • Regulation Number: 21 FR 864.5220 • Product Code: PMG
Assay Methodology	Absorbance spectrophotometry	Same
Assay Menu (FDA Cleared Assays)	Hb determination	Same
Results Reporting	Total Hb concentration	Same
Sample Type	Whole blood	Same
Sample Volume	50 µL whole blood 40 µL pre-dilute	1-2 drops venous or capillary whole blood
Sample Preparation	Manual placement of blood tube onto sample aspiration arm	Manual introduction of venous or capillary blood onto BD FACSPresto Cartridge
Sample Analysis	<ul style="list-style-type: none"> • Narrow-spectrum LED light is directed through the blood sample to measure light absorbance at a hemoglobin-absorbing wavelength. • Sodium lauryl sulfate lyses the blood cells in the sample, eliminating light attenuation caused by scatter. • Absorbance at the LED wavelength is used to calculate hemoglobin concentration. 	<ul style="list-style-type: none"> • Broad-spectrum LED light is directed through the blood sample and a diffraction grating to create a spectrum and measure light absorbance at 2 wavelengths: a hemoglobin isosbestic point and a non-hemoglobin-absorbing point. • The light absorbance in the non-hemoglobin-absorbing region measures the amount of light attenuation due to scatter. • Absorbance at the isosbestic point is corrected for scatter and used to calculate hemoglobin concentration.
Assay Principles	Photometric method with reagent that releases hemoglobin from red cells and forms a stable colored complex.	Photometric method that detects the presence of predominant forms of Hb, with correction for scatter.
Optics Principles - Hb	Absorbance photometric method using LED-generated monochromatic light and a photosensor	Absorbance spectrophotometric method using LED-generated broad spectrum light, diffraction grating, and CCD sensor
Fluidics	A vacuum pump aspirates sample blood, which passes through a rotor valve and then to volumetric dispensing, mixing, rinsing, and draining. Sample is flowing during data acquisition.	Cartridge contains a microfluidic channel through which the sample fills by capillary action. After filling completes, sample is static during data acquisition.
Instrument Setup and Quality	Setup: Automated startup check. Instrument QC: Levey -Jennings control that uses data from a single analysis of	Setup: Automated instrument setup. Instrument QC: automated verification of instrument performance at power-on-self-

Feature/ Attribute	Sysmex Automated Hematology Analyzer KX-21N (Reference Device, K981761)	BD FACSPresto System for use with BD FACSPresto CD4/Hb Cartridge and BD FACSPresto CD4/Hb Cartridge Kit (Subject Device)
Control	control sample (Sysmex Eight-Check 3WP X-Tra Controls).	test (POST) and during cartridge runs.
Software	Integrated Sysmex Software	Integrated BD FACSPresto Software

Table 5-3: Similarities/Differences – Predicate Device (R&D Systems’ Whole Blood Flow Control) against Subject Device (BD Multi-Check Control)

Feature/ Attribute	R&D Systems’ Whole Blood Flow Control (aka StatusFlow) (Predicate Device, K961610 & BK990005)	BD Multi-Check Control (Subject Device)
Intended Use/ Indications for Use	R&D Systems’ Whole Blood Flow Control (WBFC) is a stabilized preparation of human peripheral leukocytes and erythrocytes to be used as a control in the complete immunophenotyping process which includes: antibody staining, RBC lysis, instrument set-up and instrument performance.	The BD Multi-Check control is intended as a complete process control for immunophenotyping by flow cytometry. It is a control for antibody staining, red blood cell (RBC) lysis, instrument setup, instrument performance, and data analysis. The BD Multi-Check control is also intended as a CD4 and %CD4 process control for antibody staining, instrument performance, and data analysis on the BD FACSPresto system, an imaging cytometer.
Product Code	GKZ	JPK
Composition	Human leukocytes and erythrocytes in a stabilizing medium.	Same
Storage Conditions	2-8°C	Same
Open Vial Stability	9 thermal cycles	Same
Closed Vial Stability	45 days	Same

Table 5-4: Similarities/Differences – Predicate Device (StatusFlow^{Lo}) against Subject Device (BD Multi-Check CD4 Low Control)

Feature/ Attribute	StatusFlow^{Lo} (Predicate Device, K982231)	BD Multi-Check CD4 Low Control (Subject Device)
Intended Use/ Indications for Use	StatusFlow ^{Lo} is intended as a complete process control for immunophenotyping by flow cytometry. It is a control for antibody staining, RBC lysis, instrument set-up, instrument performance and data analysis.	The BD Multi-Check CD4 low control is intended as a complete process control for immunophenotyping by flow cytometry. It is a control for antibody staining, red blood cell (RBC) lysis, instrument setup, instrument performance, and data analysis. The BD Multi-Check CD4 low control is also intended as a CD4 and %CD4 process control for antibody staining, instrument performance, and data analysis on the BD FACSPresto system, an imaging cytometer.
Product Code	GKZ	JPK
Composition	Human leukocytes and erythrocytes in a stabilizing medium.	Same
Storage Conditions	2-8°C	Same
Open Vial Stability	9 thermal cycles	Same
Closed Vial Stability	45 days	Same

Table 5-5: Similarities/Differences – Predicate Device (Eurotrol Hb 301 Control) against Subject Device (Eurotrol FACSPresto Hb Control)

Feature/ Attribute	Eurotrol Hb 301 Control (Predicate Device, BK030067)	Eurotrol FACSPresto Hb Control (Subject Device)
Intended Use/ Indications for Use	The Eurotrol 301 Hb Control is an assayed hemoglobin control intended for professional use in the verification of the precision and accuracy of the HemoCue Hb 301 System.	The Eurotrol FACSPresto Hb Control is an assayed hemoglobin control intended for in vitro diagnostic use in the verification of the precision and accuracy of the BD FACSPresto System.
Product Code	GGM	JPK
Composition	Purified bovine hemolysate	Same
Open Vial Stability	30 days at 2-30°C	30 days at 2-8°C
Closed Vial Stability	25 months at 2-8°C	1 month at 2-8°C

5.9 Bench and Clinical Performance Data

The following bench performance data (**Table 5-6**) were provided in support of the substantial equivalence determination.

Table 5-6: Bench Performance Summary

Performance Characteristic	Standard	Results
Method Comparison	Based on <i>Method Comparison and Bias Estimation Using Patient Samples</i> , CLSI document EP9-A2-IR.	All method comparison results met study acceptance criteria. The BD FACSPresto system provided CD4 and %CD4 results (VP, N = 107 and FS, N = 84) that are substantially equivalent to those generated by the predicate system. The BD FACSPresto system provided Hb results (VP, N = 84 and FS, N = 108) that are substantially equivalent to those generated by the reference system.
Precision	Based on <i>Evaluation of Precision Performance of Quantitative Measurement</i> , CLSI document EP5-A2.	The BD FACSPresto system demonstrates acceptable CV and/or SD results for within-run and total precision for CD4, %CD4, and Hb measured using Streck CD-Chex Plus (Normal and CD4-Low) (N = 168) and Eurotrol FACSPresto Hb Controls (Levels 1-3) (N = 252) on the BD FACSPresto system.
Linearity	Based on <i>Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach</i> , CLSI document EP6-A.	The verification test results for the BD FACSPresto system demonstrate acceptable linearity for CD4, Lymphocyte, and Hb ranges (N = 33 for each). The dynamic range of the BD FACSPresto system is established to be linear within 42-4872 CD4 cells/ μ L. The dynamic range of the BD FACSPresto system is established to be linear within 124-10,713 Lymphocyte cells/ μ L. The dynamic range of the BD FACSPresto system is established to be linear within 2-26 Hb g/dL.
Hemoglobin Assay Traceability	Based on <i>Reference and Selected Procedures for the Quantitative Determination of Hemoglobin in Blood</i> , CLSI document H15-A3	This study concludes that the BD FACSPresto system Hb assay is traceable to the HiCN method for hemoglobin determination (N = 4-20 depending on bin). The Hb assay is linear and accurate across the reported linear range (2-20 g/dL) as compared to the HiCN method.
Analytical Sensitivity	Based on <i>Protocols for Determination of Limits of Detection and Limits of Quantitation</i> , CLSI document EP17-A	From this CD4 evaluation, the LoD is determined to be 22 cells/uL (N = 60) and the LoQ is determined to be 35 cells/uL (N=180). This LoD value is below the system's claimed range for CD4. From this Hb evaluation, the LoD is determined to be 0.91 g/dL (N=300) and the LoQ is determined to be 2 g/dL (N = 60), which supports the claimed range of 2-20 g/dL.

Performance Characteristic	Standard	Results
Interference	Based on <i>Interference Testing in Clinical Chemistry</i> , CLSI document EP7-A2.	Of the 34 analytes tested, there was no clinically significant interference at the maximum concentrations tested for 33 of them. One analyte (Gamma Globulin) demonstrated interference at the maximum concentration, but not the mid and low concentrations. None of the analytes caused a bias of > 15% with CD4, %CD4, and Hb assays in the BD FACSPresto Cartridge at the concentrations to be reported.
Specimen Stability – Age of Blood / Age of Stain	Based on <i>Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens</i> , CLSI document H04-A6	The acceptance criteria were met for all parameters. The Stability Evaluation study supports one (1) hour stain for both venous and capillary blood, and the 22-hour age of blood for venous blood only (N = 70).
Biocompatibility	<ul style="list-style-type: none"> • ANSI/AAMI/ISO 10993-5:2009, Biological Evaluation of Medical Devices-Part 5: Test for in vitro cytotoxicity • ASTM F2148:2007 – Standard Practice for Evaluation of Delayed Contact hypersensitivity using the Murine Local Lymph Node Assay (LLNA) • ANSI/AAMI/ISO 10993-10:2010, Biological Evaluation of Medical Devices-Part 10: Tests for irritation and skin sensitization 	<p>In the 48-hour titration cytotoxicity / elution test, the test article passed based on reactions observed. The test article met the requirements of the test, since the cultures treated with the extract showed no reactivity.</p> <p>In the murine local lymph node assay, the group treated with the test article elutes showed a Stimulation Index <3 compared to that of the negative control. The test article met the requirements of the test and is considered to be a non-sensitizer in mice.</p> <p>In the primary dermal irritation study, a PII score of 0 meant that the test article is considered to be a negligible irritant in rabbits.</p>
EMC	<ul style="list-style-type: none"> • IEC 61326-1:2012 • IEC61326-2-6:2012 • IEC 61000-3-2:2005 • IEC 61000-3-3:2008 	EMC testing was conducted on the BD FACSPresto System. The system complies with the IECs standards listed.
Electrical Safety	<ul style="list-style-type: none"> • UL 61010-1:2004 • IEC 61010-2-081:2002 • IEC 61010-2-101:2009 	Electrical safety testing was conducted on the BD FACSPresto System. The system complies with standards listed.
BD Multi-Check controls - Value Assignment Verification	N/A	FACSPresto-assigned ranges were established for 3 lots of BD Multi-Check Control and CD4 Low Control using 3 instruments and 3 lots of Cartridges. Data collected on 3 instruments after 18 minutes and 2 hours of incubation on the Cartridge. All data points fell within the FACSPresto-assigned ranges.

Performance Characteristic	Standard	Results
BD Multi-Check controls - Precision	Based on <i>Evaluation of Precision Performance of Quantitative Measurement</i> , CLSI document EP5-A3.	The BD Multi-Check Control and CD4 Low Control demonstrate acceptable SD and/or CV results for within-run, between-run, and total precision for CD4 and %CD4 measurements on the BD FACSPresto system. A total of 21 days and 9 open/close thermal cycles were executed for each process control lot at 3 sites and each cartridge was read within 18-30 minutes of incubation. The results of this study, with upper 97.5% confidence interval, all pass the acceptance criteria.
Eurotrol FACSPresto Hb Control - Value Assignment Verification	N/A	FACSPresto-assigned ranges were established for 3 lots of each of 3 levels with a replicate of N=9. Data collected both in-house and at 3 clinical sites were organized into three distinct sets of Level 1, Level 2, and Level 3. All data points fell within the FACSPresto-assigned ranges.
Eurotrol FACSPresto Hb Control - Precision	Based on <i>Evaluation of Precision Performance of Quantitative Measurement</i> , CLSI document EP5-A2.	The Eurotrol FACSPresto Hb Control demonstrates acceptable CV results for within-run, between-run, and total precision for Hb measurements on the BD FACSPresto system. Each cartridge was read at 3 different stain times of 1-5 minutes, 18-30 minutes and 2 hours (+/- 15 min) for a total of 240 readings per lot. With 9 lots of controls (3 lots per level), the total number of cartridges was 720 and the total number of readings with 3 stain times was 2160.

The following clinical performance data (**Table 5-7**) were provided in support of the substantial equivalence determination.

Table 5-7: Clinical Performance Summary

Performance Characteristic	Standard	Results
Method Comparison	Based on <i>Method Comparison and Bias Estimation Using Patient Samples</i> , CLSI document EP9-A2-IR.	De-identified and delinked prospectively enrolled normal and HIV infected subjects from 8 clinical sites were studied (N=796 venous and N=692 capillary). The acceptance criteria for CD4, %CD4, and Hb in venous and capillary whole blood on the BD FACSPresto system were successfully met both for all sites. No adverse effects or complications were observed.

Performance Characteristic	Standard	Results
Precision	Based on <i>Evaluation of Precision Performance of Quantitative Measurement</i> , CLSI document EP5-A2.	The precision evaluation of the BD FACSPresto system was conducted at one clinical site. The evaluation included analysis for both precision reproducibility and repeatability. Precision reproducibility measured operator and instrument variability. Site-to-site reproducibility was carried out at three clinical sites. The acceptance criteria for precision repeatability, reproducibility, and site-to-site reproducibility requirements were met for CD4, %CD4, and Hb.
Linearity	Based on <i>Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach</i> , CLSI document EP6-A.	The study was carried out at a single site using prospectively procured specimens tested on the BD FACSPresto system. For each parameter, low and high concentration pools were created from a specimen, and then the pools were proportionally mixed to achieve eleven concentrations over a range that was 20-30% wider than the anticipated claim range in addition to the CD4 medical decision point. The acceptance criteria for CD4, Lymphocytes, and Hb in the BD FACSPresto system linearity evaluation were successfully passed. Results support the linearity product claims.
Sample Stability	Based on <i>Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens</i> , CLSI document H04-A6	The BD FACSPresto system acceptance criteria for CD4, %CD4, and Hb in venous and capillary samples were successfully passed. Results from the stability evaluation support the product claims for 1 hour staining for both capillary and venous specimen types and up to 22 hours of venous blood storage.
Reference Intervals	Based on <i>Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory</i> , CLSI document EP28-A3c.	The objective of the study was to establish the CD4, %CD4, and Hb reference intervals in a normal reference cohort free of hematology abnormalities using the BD FACSPresto system in prospectively procured venous and capillary blood specimens under voluntary informed consent from adults. The final reference ranges are partitioned by parameter and gender.
BD Multi-Check Control Validation	N/A	Clinical Validation data was collected at 3 clinical trial sites to validate that the BD Multi-Check Control and CD4 Low Control fell within the FACSPresto-specific ranges. Testing at each site was performed for a minimum of 20 days. The study design incorporated at least 3 different lots of controls, instruments, and reagents. Precision of the daily runs were analyzed to monitor the control stability over time. At least 95% of the data points fell within the FACSPresto-assigned ranges.

Performance Characteristic	Standard	Results
Eurotrol FACSPresto Hb Control Validation	N/A	Clinical Validation data was collected at 3 clinical trial sites to validate that the Eurotrol FACSPresto Hb controls fall within the FACSPresto-specific ranges. Testing at each site was performed over 10 days using 3 different lots of Eurotrol FACSPresto Hb controls per level, one lot of levels 1, 2, 3 assigned per site, using one instrument at each site with one cartridge lot. Testing was done in two runs separated by a minimum of 2 hours, using duplicate samples of the three levels of Eurotrol. Precision of the daily runs were analyzed to monitor the control stability over time. All data points fell within the FACSPresto-assigned ranges.

Based on the performance data from the bench and clinical sites, the BD FACSPresto system was found to have a safety and effectiveness profile that is similar to the predicate and reference devices and raises no new issues of safety and effectiveness.

5.10 Conclusion

Based on the similar principles of operation, bench performance data, and clinical performance data, the BD FACSPresto system is substantially equivalent to the predicate BD FACSCalibur system and to the reference Sysmex system. The process controls, namely the BD Multi-Check Control and CD4 Low Control and to the Eurotrol FACSPresto Hb Controls, are substantially equivalent to the predicate StatusFlow, StatusFlow^{Lo}, and Eurotrol Hb 301 Control, respectively.