March 2, 2018

Roche Diagnostics Hematology, Inc.
Dan Bracco
Head of Clinical and Regulatory Affairs
69 Milk Street, Suite 120
Westborough, Massachusetts 01581

Re: K171655
Trade/Device Name: cobas m 511 integrated hematology analyzer
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated differential cell counter
Regulatory Class: Class II
Product Code: GKZ, JOY
Dated: June 2, 2017
Received: June 5, 2017

Dear Dan Bracco:

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 Part 801 and Part 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.

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.

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

Sincerely,

Leonthena R. Carrington -S

Lea Carrington
Director
Division of Immunology
and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K171655

Device Name
cobas m 511 integrated hematology analyzer

Indications for Use *(Describe)*
The cobas m 511 integrated hematology analyzer is a quantitative, automated analyzer with cell locating capability. It is intended for in vitro diagnostic use by a skilled operator in the clinical laboratory. The system prepares a stained microscope slide from EDTA-anticoagulated whole blood. It utilizes computer imaging to count the formed elements of blood and provide an image-based assessment of cell morphology, which may be reviewed by the operator, and also allows for manual classification of unclassified cells. The instrument reports the following parameters: RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, %NRBC, #NRBC, WBC, %NEUT, #NEUT, %LYMPH, #LYMPH, %MONO, #MONO, %EO, #EO, %BASO, #BASO, PLT, MPV, %RET, #RET, HGB-RET.

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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cobas m 511 integrated hematology analyzer
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

In accordance with 21 CFR 807.87, Roche Diagnostics Hematology, Inc. (RDH) hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification 510(k).

The purpose of this traditional 510(k) Premarket Notification is to obtain FDA review and clearance for the **cobas m** 511 integrated hematology analyzer (**cobas m** 511 system).

Submitter Name	Roche Diagnostics Hematology, Inc.
Address	69 Milk Street Suite 120 Westborough, MA 01581
Contact	Dan Bracco Phone: (508) 329-2455 FAX: (508) 329-2486 Email: dan.bracco@roche.com
Date Prepared	February 22, 2018
Proprietary Name	**cobas m** 511 integrated hematology analyzer
Common Name	Automated Differential Cell Counter Automated Cell Locating Device
Classification Name	21 CFR 864.5220, Differential Cell Counter, Class II 21 CFR 864.5260, Automated Cell Locating Device, Class II
Product Codes, Regulation Numbers	GKZ JOY
Predicate Devices	Sysmex® XN-Series (XN-10, XN-20) Automated Hematology Analyzer CellaVision® DM1200 Automated Hematology Analyzer
Establishment Registration	The establishment registration number for Roche Diagnostics Hematology has not yet been established.

1. DEVICE DESCRIPTION

The **cobas m** 511 system is a fully automated stand-alone hematology analyzer with integrated slide making capability and digital cell imaging. It provides a complete blood count, 5-part differential, and reticulocyte enumeration of samples of whole blood collected in K_2 or K_3 EDTA. It is designed for high throughput in the clinical laboratory environment.

1.1. Instrument Components and Consumables

The **cobas m** 511 system consists of the following major components:

- The analyzer, with rack transport system for sample tubes
- Viewing stations, that can be configured as the control station or as a review station
- Associated consumables and components

The **cobas m** 511 system major components:

1.1.1. **cobas m** 511 analyzer

The **cobas m** 511 analyzer is a stand-alone hematology analyzer with integrated slide making capability and digital cell imaging. It has five (5) processing stations: sample mixing, slide printing, slide staining, slide imaging (low and high magnification), and slide output. It also includes a separate compartment, which houses the necessary consumables and waste containers.

1.1.2. **cobas m** 511 viewing station

The viewing station hardware is a computer with custom software developed by RDH that provides the graphical user interface for the system. It is designed to interface with a standard Laboratory Information System (LIS) for results reporting.

1.1.3. DigiMAC^3 stain pack

The DigiMAC³ stain pack is intended to fix and stain cells from a whole blood sample or control/calibrator material that have been applied to a slide by the **cobas m** 511 analyzer, in order to make the cells suitable for automated imaging or manual microscopy. The DigiMAC^3 stain pack is comprised of the following four (4) separate solutions, which are individually applied to each processed slide: DigiMAC^3 fix, DigiMAC^3 eosin, DigiMAC^3 methylene blue,

and DigiMAC^3 rinse. The application of these stain solutions results in a Romanowsky type stain such as typically used in hematologic evaluations of whole blood.

1.1.4. DigiMAC^3 reticulocyte

DigiMAC^3 reticulocyte is intended to stain a whole blood sample or control material before it is applied to a slide by the **cobas m** 511 analyzer, in order to make the reticulocytes suitable for automated imaging or manual microscopy. DigiMAC^3 reticulocyte is a supravital stain consisting of an aqueous solution of Azure B dye as the critical component, which condenses the reticulum in red blood cells and allows visualization of reticulocytes. Unlike the stain pack solutions that stain a prepared slide, DigiMAC^3 reticulocyte is mixed with the whole blood sample by the **cobas m** 511 analyzer prior to slide printing.

1.1.5. DigiMAC^3 wash

DigiMAC^3 wash is used to clean all specimen-contacting surfaces, including blood fluid pathways, following processing of each blood sample. This solution is unique to the **cobas m** 511 system and is comprised of detergent and preservative in an aqueous, buffered solution.

1.1.6. DigiMAC^3 clean

DigiMAC^3 clean is primarily a 0.7% sodium hypochlorite formulation, which is used to remove protein build-up from the surfaces of the **cobas m** 511 analyzer components that come in contact with blood samples.

1.1.7. DigiMAC^3 slides

The DigiMAC^3 slide is a glass substrate on which a whole blood sample or control/calibrator material is applied and stained by the **cobas m** 511 analyzer, in order to enable automated imaging or manual microscopy.

1.2. Principles of Operation

The **cobas m** 511 system uses digital morphology from an automatically produced Romanowsky stained monolayer slide, to provide the standard set of hematology parameters for the complete blood count (CBC), automated white blood cell (WBC) differential, and the enumeration of reticulocytes. This is done through the use of proprietary imaging algorithms that locate, count and evaluate red and white blood cells, platelets and nucleated red blood cells.

The **cobas m** 511 system prints a consistent sample volume (a nominal 1 uL) onto a glass microscope slide using a precision application method. In the stainer module, four reagents are applied to the cells on the slide: a fixative, an eosin stain, a methylene blue stain, and a rinse. Following staining, the slide is imaged at low magnification using a 10x lens to locate, image, and count white and red blood cells, nucleated red blood cells, and platelets. The system selects a specific number of white blood cell locations and provides their coordinates to the high magnification module for additional analysis. In the high magnification module a 50x lens is used to classify white blood cell types, evaluate red blood cells, and platelets and to evaluate cellular morphology. The white blood cells are categorized into the five (5) normal types or as unclassified cells by the instrument. This allows a skilled technologist to review images of the cells on the viewing station or to perform a full microscopic review of the slide. This 50x magnification is also used to identify and count the reticulocytes when a reticulocyte test is requested. For reticulocyte processing, an additional slide is produced from blood in the sample cup that is first incubated with a supravital stain. The cells are then printed onto the slide, stained using DigiMAC3 stain and imaged to determine the number and percentage of reticulocytes and reticulocyte hemoglobin.

Following processing, results and images can be viewed on the viewing station. The viewing station allows the operator to monitor system processes and status, and to view sample processing and results. The viewing station also allows a skilled medical technologist to perform a full white blood cell differential and a morphological review of white blood cells, red blood cells and platelets for samples requiring further review.

1.3. Modes of Operation

- Closed-tube (automated rack) mode
- Open-tube (manual) mode

1.4. Specimen Identification

Specimen identification is performed automatically by the **cobas m** 511 system through an integrated barcode reader; or manually by the operator through the use of a hand-held barcode reader or keypad.

1.5. Specimen Sampling and Handling

Samples can be introduced onto the **cobas m** 511 system using either the closed-tube (automated rack mode) or open-tube modes. In the closed-tube mode the operator loads the sample tubes into a custom rack. The rack is then mechanically transported into the **cobas m** 511 system for processing. In this mode the **cobas m** 511 system automatically mixes, aspirates, and analyzes samples while the sample caps remain intact. In the open-tube mode, the operator mixes the samples tubes individually by hand and then introduces the sample to the open-port aspiration probe presented by the **cobas m** 511 system. The operator will position the tube such that the aspiration probe is immersed into the approximate center of the blood volume.

1.6. Calibration

The DigiMAC^3 calibrator is used for calibration of the **cobas m** 511 system. The calibrator is a stable suspension of cells of human or animal origin. It is used for calibrating the following hematology parameters of the **cobas m** 511 system: WBC, RBC, MCH, MCV, PLT, and MPV.

1.7. Quality Control

DigiMAC^3 controls are used to monitor the performance of the **cobas m** 511 system. These hematology quality control (QC) materials consist of stable suspensions of cells of human or animal origin. They are used for evaluating the accuracy and precision of all hematology parameters of the **cobas m** 511 analyzer. There are three (3) levels of controls (L1, L2 and L3), which are used in conjunction with each other for monitoring the performance of the **cobas m** 511 analyzer.

1.8. Software

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

2. INTENDED USE

2.1. Indication(s) for Use

The cobas m 511 integrated hematology analyzer is a quantitative, automated analyzer with cell locating capability. It is intended for in vitro diagnostic use by a skilled operator in the clinical laboratory. The system prepares a stained microscope slide from EDTA-anticoagulated whole blood. It utilizes computer imaging to count the formed elements of blood and provide an image-based assessment of cell morphology, which may be reviewed by the operator, and also allows for manual classification of unclassified cells. The instrument reports the following parameters: RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, %NRBC, #NRBC, WBC, %NEUT, #NEUT, %LYMPH, #LYMPH, %MONO, #MONO, %EO, #EO, %BASO, #BASO, PLT, MPV, %RET, #RET, HGB-RET.

2.2. Special Conditions for Use Statement(s):

For prescription use only

3. SUBSTANTIAL EQUIVALANCE INFORMATION

3.1. Predicate Device Names(s) and 510(k) numbers

Sysmex® XN-Series (XN-10, XN-20) Automated Hematology Analyzer (Sysmex Analyzer) – K112605

CellaVision® DM1200 Automated Hematology Analyzer (CellaVision Analyzer) – K092868

3.2. Comparison with Predicate Device

Table 1 compares the **cobas m** 511 system with its predicate device.

Table 1: Comparison with Predicate Device

Item	Submitted Device: cobas m 511 system	Predicate Device: Sysmex Analyzer
Indications for use	The **cobas m** 511 integrated hematology analyzer is a quantitative, automated analyzer with cell locating capability. It is intended for in vitro diagnostic use by a skilled operator in the clinical laboratory. The system prepares a stained microscope slide from EDTA-anticoagulated whole blood. It utilizes computer imaging to count the formed elements of blood and provide an image-based assessment of cell morphology, which may be reviewed by the operator, and also allows for manual classification of unclassified cells. The instrument reports the following parameters: RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, %NRBC, #NRBC, WBC, %NEUT, #NEUT, %LYMPH, #LYMPH, %MONO, #MONO, %EO, #EO, %BASO, #BASO, PLT, MPV, %RET, #RET, HGB-RET.	The XN-Series modules (XN-10, XN-20) are quantitative multi-parameter automated hematology analyzers intended for *in vitro* diagnostic use in screening patient populations found in clinical laboratories. The XN-Series modules classify and enumerate the following parameters in whole blood: WBC, RBC, HGB, HCT,MCV, MCH, MCHC, PLT (PLT-I, PLT-F), NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, IG%/#, RDW-CV, RDW-SD, MPV, NRBC%/#, RET%/#, IPF, IRF, RET-He and has a Body Fluid mode for body fluids. The Body Fluid mode enumerates the WBC-BF, RBC-BF, MN%/#, PMN%/#, and TC-BF# parameters in cerebrospinal fluid (CSF),serous fluids (peritoneal, pleural) and synovial fluids. Whole blood should be collected in K_2 or K_3 EDTA anticoagulant and, Serous and Synovial fluids in K_2 EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with CSF specimens is neither required nor recommended.
Conditions for use	For prescription use.	Same
Principle of operation	Characterizes and identifies cells using digital imaging of stained cells on a microscope slide.	Characterizes and identifies cells based on detection of direct-current resistance light scatter, fluorescence, and adaptive cluster analysis.
	Low magnification location and imaging of white and red blood cells and platelets using a 10x objective, combined with illumination optics and a camera. High magnification imaging of white blood cell types and cell morphology using a 50x objective, combined with illumination optics and a camera.	Flow cytometry method using a semiconductor laser to analyze physiological and chemical characteristics of cells and other biological particles Hydro Dynamic Focusing (DC Detection) with aperture to count the RBC and PLT and calculate the HCT via the RBC pulse height detection method.
	Hemoglobin measurement using LED light absorption	SLS-Hemoglobin Method using hemoglobin absorption after chemical lysing and LED light.

Item	Submitted Device: cobas m 511 system	Predicate Device: Sysmex Analyzer
	Automatically classifies cells from whole blood and carries out all processes from aspiration of sample to outputting of results.	Automatically classifies cells from whole blood and carries out all processes automatically from aspiration of the sample to outputting of results.
	Displays analysis results and graphics on a computer screen.	Same
	Results can be printed on available printer or transmitted to a host computer.	Same
Modes of operation	Closed-tube (automated rack) mode Open-tube (manual) mode	Sampler Analysis Mode (Closed Cap) Manual Analysis Mode (Closed and Open Cap) Pre-dilute Analysis Mode Low WBC Analysis Mode Body Fluid Mode
Methodology	Performs automated analyses of whole blood cells using a combination of low and high magnification computer imaging of stained cells.	Performs hematology analyses according to the Hydro Dynamic Focusing (DC Detection), flow cytometry method (using semiconductor laser), and SLS-hemoglobin method.
Sample identification	Automated barcode reading of sample tube identifier. Manual keyboard entry. Bi-directional instrument to LIS interface: patient demographics, orders, results.	Same
Calibrator	Calibration and verification of calibration using stabilized whole blood calibrator.	Same
	DigiMAC^3 calibrator	XN CAL (for WBC, RBC, HGB, HCT, PLT and RET) XN CAL PF (for PLT-F)
Quality control	Three (3) stabilized whole blood control levels of varying component concentrations.	Same
	DigiMAC^3 control L1 DigiMAC^3 control L2 DigiMAC^3 control L3	XN Check (3 levels)
Sample types	Whole blood	Same Body Fluids
Anticoagulant	K_2 and K_3 ethylenediaminetetraacetic acid (EDTA)	Same
Sample collection device	Evacuated blood collection tube containing EDTA as an anticoagulant.	Same
Quality control techniques	Levey-Jennings control chart X-bar charting	Same

Item	Submitted Device: **cobas m 511 system**	Predicate Device: **Sysmex Analyzer**
Intended use population	All whole blood samples from any individual sent to laboratory for analysis.	Same, also including body fluids
Sample aspiration volume	30µL (closed-tube and open-tube mode)	88µL (Sampler Mode-Whole Blood) 88µL (Manual Mode- Whole Blood) 70µL (Manual Mode- Diluted Blood)
Service diagnostics	On-board system diagnostics Manufacturer can perform web-based diagnostics.	Same
Throughput	Approximately 60 samples/hour maximum	Approximately 100 samples/hour maximum
Reagents	DigiMAC^3 stain pack, including: DigiMAC^3 fix (fixative) DigiMAC^3 eosin (stain) DigiMAC^3 methylene blue (stain) DigiMAC^3 rinse (rinse) DigiMAC^3 reticulocyte (stain)	CELLPACK DCL (Diluent) CELLPACK DFL (Diluent) LYSERCELL WNR (Lyse) LYSERCELL WDF (Lyse) LYSERCELL WPC (Lyse) FLUOROCELL WNR (Stain) FLUOROCELL WDF (Stain) FLUOROCELL RET (Stain) FLUOROCELL PLT (Stain) FLUOROCELL WPC (Stain) SULFOLYSER (Lyse)
Cleaning solutions	DigiMAC^3 wash DigiMAC^3 clean	CELLCLEAN AUTO
Software	Analyzer OS: Linux Viewing Station OS: MacOS	Microsoft Windows
	Proprietary **cobas m** 511 software	Proprietary Sysmex software
Analysis technique	Instrument measures targeted parameters automatically. Examiner can assess results via viewing screen or printed report.	Same
Number of samples	Multiple maintained in queue. One sample result presented at a time.	Same
Number of individuals represented per sample	One	Same
Presentation of abnormal samples	Results reported numerically with flags.	Same
Analyte targets	Components of cells such as DNA, RNA and proteins	Same
Sample preparation procedure	Printing of blood onto a microscope slide followed by staining of the slide.	Flow analysis after dilution and mixing with reagents.
Light sources	Light Emitting Diodes (LEDs)	Semiconductor Laser
Operational conditions	18 to 27°C ambient temperature 20-60% relative humidity	15 to 30°C ambient temperature 20-85% relative humidity

Item	Submitted Device: cobas m 511 system	Predicate Device: Sysmex Analyzer
Automation	Transportation of racks of sample tubes on conveyor.	Same
Sample handling system	Individual sample tubes are automatically removed from rack to be processed. Manual open-tube mode.	Same
Reagent access	Reagent (cleaning solution) and slides stored within the instrument and remaining reagents stored in a drawer within the instrument below the analytical components.	Reagents stored within the top front cover of the instrument and in a cabinet below the analyzer.
Reagent bottle/Cartridge identification	Barcodes	Barcode or reagent specific cassette position
Reagent mixing	No reagent mixing required.	Same
Information transfer to and from instrument	Through LIS or manual entry on a computer screen.	Same
Probe cleaning	Automatically for each specimen and periodically with special clean reagent.	Same
Host interface	LIS or middleware	Same
Calibration intervals	Performed by manufacturer at installation and as needed.	Same
Stain types	Absorbent dyes, hemoglobin absorption with LED light.	Fluorescent dyes, hemoglobin absorption with chemical lysing and semiconductor laser beam light.
User management	Allows setting of user assignment and level of access.	Same
Flagging of errors or sample conditions	System and sample errors and messages are configurable, displayed and reported by system to the LIS.	Same

Table 2 compares the **cobas m** 511 system with its predicate device, CellaVision Analyzer.

Table 2: Comparison with CellaVision Analyzer

Item	Submitted Device: cobas m 511 system	Predicate Device: CellaVision Analyzer
Indications for use	The **cobas m** 511 integrated hematology analyzer is a quantitative, automated analyzer with cell locating capability. It is intended for in vitro diagnostic use by a skilled operator in the clinical laboratory. The system prepares a stained microscope slide from EDTA-anticoagulated whole blood. It utilizes computer imaging to count the formed elements of blood and provide an image-based assessment of cell morphology, which may be reviewed by the operator, and also allows for manual classification of unclassified cells. The instrument reports the following parameters: RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, %NRBC, #NRBC, WBC, %NEUT, #NEUT, %LYMPH, #LYMPH, %MONO, #MONO, %EO, #EO, %BASO, #BASO, PLT, MPV, %RET, #RET, HGB-RET.	DM1200 is an automated cell-locating device. DM1200 automatically locates and presents images of blood cells on peripheral blood smears. The operator identifies and verifies the suggested classification of each cell according to type. DM1200 is intended to be used by skilled operators, trained in the use of the device and in recognition of blood cells.
Principle of operation	Low magnification location and imaging of white and red blood cells and platelets. High magnification imaging of white blood cell types and cell morphology. Displays analysis results, graphics, and images on a computer screen. Results can be printed on available printer or transmitted to a host computer.	The analysis process consists of an overview image processing and a cell-location step. The overview image is used to find cells of interest and to obtain an overall impression of the sample. The overview image can have one 10x zoom level or both 10x and 50x zoom levels. The cell-location step uses the optical unit and a camera to obtain images of the identified images and stores the images in a database.
Methodology	Performs automated analyses of whole blood cells using a combination of low and high magnification imaging of stained cells on a glass microscope slide, with subsequent operator review of computerized images or glass microscope slide for flagged cases.	Same
Sample identification	Automated barcode reading of sample identifier. Manual keyboard entry.	Same
Specimen types	Whole Blood	Same Body Fluids

Item	Submitted Device: cobas m 511 system	Predicate Device: CellaVision Analyzer
Sample preparation	Automated slide preparation and staining.	Automated or manual slide preparation and staining.
Stains	Romanowsky type stain	Same
Analysis technique	Locates, identifies, and counts the various types of white blood cells under the automated microscope. Red blood cells and platelets and platelet morphology can be assessed by examiner.	Same
Presentation of samples	Results reported numerically. Cells can be observed on a computer display. Cells can be observed through a microscope.	Same
Handling of abnormal samples	Images automatically made available for review. Slides available as needed for subsequent review.	Same
Analyte targets	Stained components of cells such as DNA, RNA, and proteins.	Same
Light sources and detector	LED light sources with specific Blue, Green, Yellow and Red wavelengths.	White light source.
	Black and White cameras.	Color camera with RGB filters on individual pixels.
Automation	Slides moved automatically through system.	Same
Sample identification	Analyzer tracks slide location in system and prints alphanumeric sample identification on slide.	Barcode identification on slide.
Measurement principle	Numeric morphologic features from digital images and cell type computer classification.	Same
Information transfer to/from instrument	Through LIS or manual entry on a computer screen.	Same
Internal quality management system	System performs self-testing and light adjustment. Quality control samples run daily.	Same
Calibration intervals	Performed at installation and as needed.	Same
Display	Restricted to Apple iMac computer with specific integrated display size, resolution, and color specifications.	Various
Intrinsic color compensation	Algorithms and classifiers tolerate stain variations.	Same

Item	Submitted Device: **cobas m 511 system**	Predicate Device: **CellaVision Analyzer**
	Display color cannot be adjusted.	Display color can be adjusted.
Software	Analyzer OS: Linux Viewing Station OS: MacOS	Microsoft Windows
	Proprietary **cobas m** 511 software	Proprietary software
Result and image storage	Stores results and images in a local database.	Same

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

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

CLSI EP07-A2 Interference Testing In Clinical Chemistry; Approved Guideline - Second Edition

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

CLSI EP10-A3-AMD Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures, Approved Guideline - Third Edition

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

CLSI EP28-A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition

CLSI H20-A2	Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard - Second Edition
CLSI H26-A2	Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard - Second Edition
IEC 61010-1:2010	Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements
IEC 61010-2-101:2015	Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment
IEC 61326-1:2012	Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 1: General requirements
IEC 61326-2-6:2012	Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 2-6: Particular requirements - In vitro diagnostic (IVD) medical equipment
IEC 62304:2006	Medical device software – Software life cycle processes
ISO 14971:2007	Medical devices – Application of risk management to medical devices

5. PERFORMANCE CHARACTERESTICS

5.1. Analytical Performance

5.1.1. Method Comparison

A method comparison study was performed to compare results of residual whole blood samples that were randomly collected for a minimum of two (2) weeks at each of four (4) clinical sites. Specific interference samples and medical decision level samples were also included at each site. Each sample was processed on the **cobas m** 511 system and the predicate device within eight (8) hours of venipuncture. Correlation and bias between the **cobas m** 511 system and the comparator analyzer were determined in accordance with the CLSI EP09-A3 guideline based on the results of either a Passing-Bablok or Deming regression model. For the %NRBC and #NRBC parameters the mean difference was used to calculate bias in accordance with the CLSI EP09-A3 guideline. If a parameter has mixed acceptance criteria comprised of both an absolute bias limit and a proportional bias limit, the bias has been reported at the crossover point where the two (2) bias limits are equal. In these cases the crossover point is listed in both absolute and proportional terms for the same value. Because bias is calculated using a linear model, if the calculated bias was found to be acceptable at the low bias limit, high bias limit, and crossover point (if required), the bias is considered acceptable at all points in between. The results of the Method Comparison evaluation were found to be acceptable for all reportable parameters. The results for all sites combined are shown in Table 3.

Table 3: Summary of cobas m 511 system vs. Predicate Device for All Sites Combined

Parameter [Units]	N	Pearson's (r)	Intercept (95% CI)	Slope (95% CI)	Sample Range	Evaluation Range			Bias (95% CI)			
						Low End	Crossover Point	High End	At Low Limit	Crossover Point		At High Limit
WBC [10^3/µL]	1859	0.999	0.02 (-0.01, 0.05)	1.012 (1.007, 1.017)	(0.04, 247.04)	0.50	4.00	30.00	0.03 (0.00, 0.05)	0.07 (0.05, 0.08) [10^3/µL]	1.7 (1.34, 2.09) [%]	1.26 (0.87, 1.69)
RBC [10^6/µL]	1859	0.974	0.02 (-0.01, 0.04)	0.991 (0.985, 1.000)	(1.15, 7.21)	4.00	N/A	5.50	-0.41 (-0.59, -0.25)	N/A		-0.56 (-0.82, -0.18)
HGB [g/dL]	1853	0.970	-0.33 (-0.41, -0.24)	1.046 (1.039, 1.053)	(4.20, 21.20)	4.50	10.00	21.20	-0.12 (-0.17, -0.07)	0.14 (0.11, 0.15) [g/dL]	1.35 (1.15, 1.53) [%]	3.08 (2.70, 3.42)
HCT [%]	1859	0.953	-0.72 (-1.06, -0.35)	1.043 (1.033, 1.053)	(13.50, 66.00)	14.00	N/A	66.00	-0.87 (-2.40, 0.71)	N/A		3.20 (2.68, 3.68)
MCV [fL]	1859	0.887	-3.03 (-5.06, -0.87)	1.060 (1.035, 1.083)	(58.20, 119.20)	80.00	N/A	100.00	2.25 (1.97, 2.58)	N/A		3.01 (2.65, 3.36)
MCH [pg]	1844	0.956	1.37 (0.73, 1.80)	0.974 (0.960, 0.996)	(17.58, 40.75)	28.00	N/A	34.00	2.33 (2.14, 2.52)	N/A		1.47 (1.19, 1.76)
MCHC [g/dL]	1844	0.559	15.71 (14.73, 16.45)	0.522 (0.500, 0.552)	(26.59, 36.80)	32.00	N/A	36.00	1.26 (1.09, 1.43)	N/A		-4.19 (-4.44, -3.92)
RDW [%]	1859	0.913	2.46 (2.15, 2.74)	0.870 (0.848, 0.892)	(10.70, 29.40)	12.00	N/A	14.60	7.43 (6.98, 7.86)	N/A		3.78 (3.39, 4.11)
RDW-SD [fL]	1859	0.912	5.48 (4.48, 6.46)	0.940 (0.917, 0.963)	(31.70, 97.10)	40.00	N/A	60.00	7.70 (7.31, 8.13)	N/A		3.13 (2.42, 3.90)
PLT [10^3/µL]	1808	0.973	-11.03 (-13.21, -8.94)	1.020 (1.008, 1.031)	(1.00, 1061.00)	10.00	75.00	1000.0	-10.83 (-12.94, -8.85)	-9.54 (-11.04, -8.10) [10^3/µL]	-12.73 (-14.72, -10.80) [%]	0.88 (-0.08, 1.84)
MPV [fL]	1678	0.772	-0.91 (-1.40, -0.20)	1.063 (1.000, 1.111)	(8.00, 13.00)	8.00	N/A	10.20	-5.08 (-6.62, -2.50)	N/A		-2.63 (-3.03, -1.96)

Parameter [Units]	N	Pearson's (r)	Intercept (95% CI)	Slope (95% CI)	Sample Range	Evaluation Range			Bias (95% CI)			
						Low End	Crossover Point	High End	At Low Limit	Crossover Point		At High Limit
%NRBC [/100 WBC]	1862	0.981	N/A	N/A	(0.00, 186.10)	0.00	N/A	1.50	-0.03 (-0.06, 0.01)	N/A		(mean difference)
#NRBC [10^3/µL]	1864	0.995	N/A	N/A	(0.00, 9.59)	0.00	N/A	0.10	0.00 (0.00, 0.00)	N/A		(mean difference)
%NEUT [%]	1585	0.989	1.62 (1.12, 2.15)	1.012 (1.004, 1.019)	(10.10, 94.00)	40.00	N/A	85.00	5.21 (4.60, 5.84)	N/A		3.06 (2.82, 3.30)
%LYMPH [%]	1648	0.989	-0.23 (-0.37, -0.08)	0.977 (0.971, 0.983)	(0.70, 83.00)	25.00	40.00	65.00	-0.81 (-0.91, -0.70)	-1.15 (-1.32, -0.98) [%LYMPH]	-2.89 (-3.30, -2.44) [%]	-2.66 (-3.13, -2.15)
%MONO [%]	1648	0.913	-0.60 (-0.82, -0.50)	1.000 (1.000, 1.026)	(0.60, 24.50)	2.00	N/A	10.00	-0.60 (-0.78, -0.50)	N/A		-0.60 (-0.70, -0.50)
%EO [%]	1702	0.973	-0.08 (-0.13, -0.03)	1.042 (1.030, 1.054)	(0.00, 32.90)	0.00	N/A	5.00	-0.08 (-0.13, -0.03)	N/A		0.13 (0.09, 0.17)
%BASO [%]	1788	0.721	-0.30 (-0.35, -0.25)	1.649 (1.576, 1.723)	(0.00, 3.10)	0.00	N/A	1.00	-0.30 (-0.35, -0.25)	N/A		0.35 (0.31, 0.39)
#NEUT [10^3/µL]	1585	0.994	0.12 (0.09, 0.15)	1.027 (1.021, 1.033)	(0.37, 37.66)	1.00	1.50	10.00	0.15 (0.12, 0.17)	0.16 (0.14, 0.19) [10^3/µL]	10.98 (9.18, 12.37) [%]	3.92 (3.43, 4.36)
#LYMPH [10^3/µL]	1648	0.990	-0.06 (-0.07, -0.05)	1.032 (1.022, 1.042)	(0.02, 12.66)	0.50	1.50	3.00	-0.04 (-0.05, -0.03)	-0.01 (-0.02, 0.00) [10^3/µL]	-0.71 (-1.30, -0.16) [%]	1.26 (0.58, 1.87)
#MONO [10^3/µL]	1648	0.940	-0.03 (-0.04, -0.02)	1.000 (0.976, 1.000)	(0.01, 6.14)	0.10	N/A	1.50	-0.03 (-0.04, -0.02)	N/A		-0.03 (-0.06, -0.03)
#EO [10^3/µL]	1702	0.976	-0.01 (-0.01, 0.00)	1.071 (1.060, 1.083)	(0.00, 7.17)	0.00	N/A	0.50	-0.01 (-0.01, 0.00)	N/A		0.03 (0.03, 0.04)
#BASO [10^3/µL]	1788	0.680	-0.02 (-0.03, -0.02)	1.661 (1.577, 1.744)	(0.00, 0.46)	0.00	N/A	0.10	-0.02 (-0.03, -0.02)	N/A		0.04 (0.04, 0.05)
%RET [%]	1842	0.964	-0.36 (-0.39, -0.32)	1.094 (1.072, 1.116)	(0.05, 12.93)	0.50	1.67	2.50	-0.31 (-0.34, -0.28)	-0.20 (-0.21, -0.18) [%RET]	-11.91 (-12.75, -10.83) [%]	-4.84 (-5.80, -3.81)

Parameter [Units]	N	Pearson's (r)	Intercept (95% CI)	Slope (95% CI)	Sample Range	Evaluation Range			Bias (95% CI)		
						Low End	Crossover Point	High End	At Low Limit	Crossover Point	At High Limit
#RET [10^6/µL]	1834	0.924	-0.01 (-0.01, -0.01)	1.070 (1.047, 1.092)	(0.00, 0.42)	0.02	N/A	0.15	-0.01 (-0.01, -0.01)	N/A	0.00 (0.00, 0.00)
HGB-RET [pg]	1701	0.793	-3.29 (-4.69, -1.94)	1.141 (1.100, 1.184)	(16.23, 45.00)	23.00	N/A	40.00	-0.23 (-2.11, 1.61)	N/A	5.84 (4.94, 6.83)

5.1.2. Flagging Capabilities

Clinical sensitivity studies were conducted at the four (4) clinical sites to evaluate cobas **m** 511 system messages (flags) for white blood cells versus a 400-cell reference method. The 400-cell reference method according to the CLSI H20-A2 standard refers to the combined results from two (2) 200-cell WBC differentials performed by individuals on two (2) separate blood smears. The samples used represented a variety of abnormal conditions. The results obtained from comparison of **cobas m** 511 system messages versus the 400-cell reference method met the acceptance criteria for sensitivity and specificity. These results are summarized in Table 4.

Table 4: Clinical Sensitivity Analysis – cobas m 511 system Messages for All Sites Combined

		cobas m 511 system		
		Positive (Flagged Abnormal)	**Negative (Normal)**	**Total**
Reference Method	**Positive (Abnormal)**	118	9	127
	Negative (Normal)	10	302	312
	Total	128	311	439

Sensitivity = 118/(118+9) x 100% = 92.9%, Specificity = 302/(302+10) x 100% = 96.8%

5.1.3. Precision

Precision studies were performed at the four (4) clinical sites to evaluate repeatability (i.e., within-run precision) when whole blood samples were processed thirty-one (31) consecutive times on the **cobas m** 511 system, as recommended in the CLSI H26-A2 standard. Residual K_2 EDTA whole blood samples spanning the upper and lower limit of the analytical measuring range generally encountered in the laboratory were selected for the WBC, RBC, HGB and PLT parameters. In addition, samples at medical decision levels of anemia, thrombocytopenia, severe leukopenia, and nucleated red blood cells were evaluated. The mean, standard deviation (SD), and coefficient of variation (CV) were calculated for each sample per the CLSI EP05-A3 guideline. Repeatability results met their pre-defined acceptance criteria. The results of the individual assessments by parameter for all sites combined are shown in Table 5.

Table 5: Repeatability Results for All Sites Combined

Parameter [Units]	Sample Range	Sample Size (N)	Observations (N)	Range of Sample Means	Mean of Sample Means	Repeatability	
						SD (95% CI)	%CV (95% CI)
WBC [10^3/µL]	All	144	4436	(1.98, 130.75)	12.06	0.233 (0.229, 0.238)	1.93 (1.89, 1.97)
	< 4.0 x 10^3/µL	17	520	(1.98, 3.95)	3.19	0.096 (0.090, 0.102)	3.01 (2.84, 3.21)
	≥ 4.0 x 10^3/µL	127	3916	(4.00, 130.75)	13.24	0.246 (0.241, 0.252)	1.85 (1.81, 1.90)
RBC [10^6/µL]	All	144	4436	(1.92, 6.40)	4.10	0.034 (0.034, 0.035)	0.84 (0.82, 0.86)
HGB [g/dL]	All	144	4436	(5.98, 20.26)	12.37	0.135 (0.132, 0.137)	1.09 (1.06, 1.11)
HCT [%]	All	144	4436	(18.39, 65.15)	37.81	0.373 (0.365, 0.381)	0.99 (0.97, 1.01)
MCV [fL]	All	144	4436	(66.36, 109.80)	92.64	0.600 (0.588, 0.613)	0.65 (0.63, 0.66)
MCH [pg]	All	144	4436	(20.16, 36.19)	30.29	0.189 (0.185, 0.193)	0.62 (0.61, 0.64)
MCHC [g/dL]	All	144	4436	(30.22, 34.47)	32.69	0.142 (0.139, 0.145)	0.43 (0.42, 0.44)
RDW [%]	All	144	4436	(12.23, 27.18)	15.24	0.277 (0.272, 0.283)	1.82 (1.78, 1.86)
RDW-SD [fL]	All	144	4436	(40.26, 83.41)	50.71	0.872 (0.854, 0.891)	1.72 (1.68, 1.76)

Parameter [Units]	Sample Range	Sample Size (N)	Observations (N)	Range of Sample Means	Mean of Sample Means	Repeatability	
						SD (95% CI)	%CV (95% CI)
PLT [10^3/µL]	All	143	4405	(14.74, 936.84)	246.77	6.749 (6.609, 6.895)	2.73 (2.67, 2.79)
	< 150 x 10^3/µL	31	950	(14.74, 149.61)	103.71	3.364 (3.217, 3.525)	3.24 (3.10, 3.40)
	≥ 150 x 10^3/µL	112	3455	(152.71, 936.84)	286.36	7.413 (7.240, 7.595)	2.59 (2.53, 2.65)
MPV † [fL]	All	141	4347	(8.76, 14.91)	10.74	0.170 (0.167, 0.174)	1.58 (1.55, 1.62)
%NRBC * [/100 WBC]	All	143	4405	(0.00, 4.09)	0.12	0.082 (0.080, 0.084)	66.68 (65.29, 68.13)
	< 4%	142	4374	(0.00, 0.97)	0.09	0.080 (0.079, 0.082)	85.04 (83.27, 86.90)
	≥ 4%	1	31	(4.09, 4.09)	4.09	0.197 (0.157, 0.263)	4.80 (3.84, 6.42)
#NRBC [10^3/µL]	All	144	4436	(0.00, 1.32)	0.02	0.009 (0.009, 0.009)	40.10 (39.27, 40.97)
	< 0.25 x 10^3/µL	142	4374	(0.00, 0.20)	0.01	0.007 (0.007, 0.007)	61.46 (60.17, 62.79)
	≥ 0.25 x 10^3/µL	2	62	(0.28, 1.32)	0.80	0.048 (0.041, 0.059)	6.06 (5.15, 7.38)
%NEUT * [%]	All	142	4365	(4.82, 96.81)	68.17	1.598 (1.564, 1.632)	2.34 (2.29, 2.39)
	< 33.3%	3	87	(4.82, 30.78)	20.80	1.749 (1.520, 2.060)	7.99 (6.94, 9.41)
	≥ 33.3%	139	4278	(35.19, 96.81)	69.19	1.594 (1.561, 1.629)	2.30 (2.26, 2.36)

Parameter [Units]	Sample Range	Sample Size (N)	Observations (N)	Range of Sample Means	Mean of Sample Means	Repeatability	
						SD (95% CI)	%CV (95% CI)
%LYMPH * [%]	All	142	4365	(1.43, 89.38)	20.94	1.406 (1.377, 1.437)	6.74 (6.60, 6.89)
	< 13.3%	43	1329	(1.43, 13.28)	7.47	0.913 (0.879, 0.949)	12.21 (11.76, 12.70)
	≥ 13.3%	99	3036	(13.47, 89.38)	26.79	1.575 (1.535, 1.616)	5.89 (5.74, 6.05)
%MONO * [%]	All	142	4365	(1.36, 21.30)	7.84	0.959 (0.939, 0.980)	12.25 (12.00, 12.52)
	< 6.67%	56	1717	(1.36, 6.65)	4.88	0.760 (0.735, 0.786)	15.56 (15.05, 16.11)
	≥ 6.67%	86	2648	(6.69, 21.30)	9.76	1.069 (1.040, 1.099)	10.97 (10.68, 11.28)
%EO * [%]	All	142	4365	(0.00, 14.66)	2.42	0.534 (0.523, 0.546)	21.96 (21.50, 22.44)
	< 4%	115	3529	(0.00, 3.97)	1.46	0.418 (0.408, 0.428)	28.61 (27.95, 29.31)
	≥ 4%	27	836	(4.09, 14.66)	6.53	0.867 (0.826, 0.911)	13.27 (12.65, 13.95)
%BASO * [%]	All	142	4365	(0.01, 2.34)	0.61	0.278 (0.272, 0.284)	45.28 (44.33, 46.26)
#NEUT * [10^3/µL]	All	142	4365	(0.87, 49.70)	7.86	0.243 (0.238, 0.248)	3.08 (3.02, 3.15)
#LYMPH * [10^3/µL]	All	142	4365	(0.21, 116.87)	2.45	0.173 (0.170, 0.177)	7.52 (7.36, 7.68)
#MONO * [10^3/µL]	All	142	4365	(0.03, 7.32)	0.79	0.132 (0.129, 0.135)	16.90 (16.55, 17.27)

Parameter [Units]	Sample Range	Sample Size (N)	Observations (N)	Range of Sample Means	Mean of Sample Means	Repeatability	
						SD (95% CI)	%CV (95% CI)
#EO * [10^3/µL]	All	142	4365	(0.00, 0.87)	0.19	0.050 (0.049, 0.051)	26.15 (25.61, 26.72)
#BASO * [10^3/µL]	All	142	4365	(0.00, 0.25)	0.05	0.028 (0.028, 0.029)	55.84 (54.67, 57.06)

* Only samples with ≥ 2.0x 10^3/µL WBC are used for calculation of repeatability of differential parameters.

† Only samples with ≥ 20 x 10^3/µL PLT are used for calculation of repeatability of MPV.

5.1.4. Reproducibility

Studies were performed to evaluate reproducibility (total precision) at the four (4) clinical sites using three (3) levels of stabilized quality control material (DigiMAC^3 control L1, L2 and L3), consistent with Chapter 4 of the CLSI EP05-A3 guideline. The assessment utilized a $4 \times 5 \times 2 \times 3$ design, where: 4 = number of clinical sites, 5 = number of run days, 2 = number of runs (i.e., batches) per day, 3 = number of replicates per run. The data generated from this study were used to calculate various components of precision, including the following: Within-Run (Repeatability), Between-Run, Between-Day, Between-Laboratory (Site), Total (Reproducibility). Acceptance criteria were applied to the Total (Reproducibility) component. Reproducibility for the three (3) levels of DigiMAC^3 controls was calculated and found to be acceptable for all sites combined for all reportable parameters. The results of this assessment for all sites combined are shown in Table 6.

Table 6: Reproducibility Test Case Results for All Sites Combined

Parameter [Units]	Control Level	N	Mean	Within-Run (Repeatability)		Between-Run		Between-Day		Between Laboratory (Site)		Total (Reproducibility)	
				SD (95% CI)	%CV (95% CI)	SD	%CV	SD	%CV	SD	%CV	SD (95% CI)	%CV (95% CI)
WBC [10^3/µL]	L1	120	16.93	0.259 (0.224, 0.306)	1.53 (1.32, 1.81)	0.000	0.00	0.151	0.89	0.272	1.61	0.404 (0.290, 0.669)	2.39 (1.71, 3.95)
	L2	120	8.00	0.209 (0.181, 0.248)	2.62 (2.27, 3.10)	0.022	0.28	0.065	0.82	0.158	1.97	0.271 (0.208, 0.391)	3.39 (2.60, 4.88)
	L3	120	2.64	0.150 (0.130, 0.177)	5.66 (4.91, 6.70)	0.000	0.00	0.077	2.93	0.096	3.64	0.194 (0.154, 0.261)	7.34 (5.85, 9.88)
RBC [10^6/µL]	L1	120	2.56	0.018 (0.016, 0.022)	0.72 (0.62, 0.85)	0.006	0.25	0.019	0.75	0.064	2.50	0.070 (0.042, 0.200)	2.72 (1.63, 7.81)
	L2	120	4.29	0.053 (0.046, 0.062)	1.23 (1.06, 1.45)	0.000	0.00	0.039	0.92	0.102	2.38	0.121 (0.077, 0.280)	2.83 (1.80, 6.53)
	L3	120	5.58	0.056 (0.049, 0.066)	1.00 (0.87, 1.19)	0.000	0.00	0.052	0.94	0.116	2.08	0.139 (0.089, 0.319)	2.50 (1.59, 5.72)
HGB [g/dL]	L1	120	6.26	0.058 (0.050, 0.068)	0.92 (0.80, 1.09)	0.014	0.22	0.050	0.79	0.216	3.45	0.230 (0.136, 0.701)	3.67 (2.17, 11.19)
	L2	120	12.31	0.143 (0.124, 0.169)	1.16 (1.01, 1.37)	0.019	0.15	0.112	0.91	0.374	3.04	0.417 (0.254, 1.117)	3.38 (2.06, 9.08)
	L3	120	17.45	0.216 (0.187, 0.256)	1.24 (1.07, 1.46)	0.000	0.00	0.145	0.83	0.461	2.64	0.530 (0.330, 1.311)	3.04 (1.89, 7.51)

Parameter [Units]	Control Level	N	Mean	Within-Run (Repeatability)		Between-Run		Between-Day		Between Laboratory (Site)		Total (Reproducibility)	
				SD (95% CI)	%CV (95% CI)	SD	%CV	SD	%CV	SD	%CV	SD (95% CI)	%CV (95% CI)
HCT [%]	L1	120	18.11	0.154 (0.134, 0.183)	0.85 (0.74, 1.01)	0.065	0.36	0.144	0.79	0.409	2.26	0.465 (0.287, 1.192)	2.57 (1.58, 6.58)
	L2	120	34.95	0.406 (0.352, 0.480)	1.16 (1.01, 1.37)	0.118	0.34	0.283	0.81	0.639	1.83	0.817 (0.541, 1.651)	2.34 (1.55, 4.72)
	L3	120	49.24	0.596 (0.516, 0.705)	1.21 (1.05, 1.43)	0.000	0.00	0.331	0.67	0.735	1.49	1.003 (0.690, 1.828)	2.04 (1.40, 3.71)
MCV [fL]	L1	120	70.77	0.305 (0.264, 0.361)	0.43 (0.37, 0.51)	0.265	0.37	0.226	0.32	0.268	0.38	0.535 (0.417, 0.744)	0.76 (0.59, 1.05)
	L2	120	81.47	0.342 (0.297, 0.405)	0.42 (0.36, 0.50)	0.356	0.44	0.239	0.29	0.474	0.58	0.725 (0.522, 1.188)	0.89 (0.64, 1.46)
	L3	120	88.27	0.413 (0.358, 0.488)	0.47 (0.41, 0.55)	0.285	0.32	0.464	0.53	0.499	0.56	0.846 (0.624, 1.316)	0.96 (0.71, 1.49)
MCH [pg]	L1	120	24.48	0.129 (0.112, 0.153)	0.53 (0.46, 0.62)	0.087	0.36	0.115	0.47	0.288	1.18	0.347 (0.222, 0.784)	1.42 (0.91, 3.20)
	L2	120	28.68	0.110 (0.095, 0.130)	0.38 (0.33, 0.45)	0.114	0.40	0.110	0.38	0.232	0.81	0.301 (0.200, 0.602)	1.05 (0.70, 2.10)
	L3	120	31.28	0.134 (0.116, 0.158)	0.43 (0.37, 0.51)	0.092	0.29	0.102	0.33	0.216	0.69	0.289 (0.196, 0.549)	0.92 (0.63, 1.75)
MCHC [g/dL]	L1	120	34.58	0.122 (0.106, 0.145)	0.35 (0.31, 0.42)	0.110	0.32	0.213	0.62	0.448	1.29	0.522 (0.326, 1.285)	1.51 (0.94, 3.72)
	L2	120	35.20	0.107 (0.093, 0.126)	0.30 (0.26, 0.36)	0.116	0.33	0.138	0.39	0.441	1.25	0.489 (0.296, 1.340)	1.39 (0.84, 3.81)
	L3	120	35.43	0.097 (0.084, 0.115)	0.28 (0.24, 0.33)	0.084	0.24	0.171	0.48	0.415	1.17	0.467 (0.285, 1.242)	1.32 (0.80, 3.51)

Parameter [Units]	Control Level	N	Mean	Within-Run (Repeatability)		Between-Run		Between-Day		Between Laboratory (Site)		Total (Reproducibility)	
				SD (95% CI)	%CV (95% CI)	SD	%CV	SD	%CV	SD	%CV	SD (95% CI)	%CV (95% CI)
RDW [%]	L1	120	15.62	0.277 (0.240, 0.328)	1.77 (1.54, 2.10)	0.090	0.57	0.060	0.38	0.236	1.51	0.379 (0.284, 0.572)	2.43 (1.82, 3.66)
	L2	120	13.18	0.248 (0.215, 0.294)	1.88 (1.63, 2.23)	0.203	1.54	0.000	0.00	0.107	0.81	0.338 (0.287, 0.410)	2.56 (2.18, 3.11)
	L3	120	13.12	0.277 (0.240, 0.328)	2.11 (1.83, 2.50)	0.000	0.00	0.028	0.21	0.112	0.86	0.300 (0.256, 0.363)	2.29 (1.95, 2.76)
RDW-SD [fL]	L1	120	39.79	0.587 (0.508, 0.694)	1.48 (1.28, 1.75)	0.307	0.77	0.263	0.66	0.744	1.87	1.030 (0.715, 1.837)	2.59 (1.80, 4.62)
	L2	120	38.65	0.628 (0.544, 0.743)	1.63 (1.41, 1.92)	0.487	1.26	0.000	0.00	0.480	1.24	0.929 (0.734, 1.266)	2.40 (1.90, 3.28)
	L3	120	41.71	0.759 (0.658, 0.898)	1.82 (1.58, 2.15)	0.000	0.00	0.211	0.51	0.449	1.08	0.907 (0.731, 1.196)	2.18 (1.75, 2.87)
PLT [10^3/µL]	L1	120	470.53	4.611 (3.994, 5.455)	0.98 (0.85, 1.16)	1.885	0.40	3.705	0.79	5.187	1.10	8.090 (5.856, 13.074)	1.72 (1.24, 2.78)
	L2	120	215.97	3.213 (2.783, 3.802)	1.49 (1.29, 1.76)	0.771	0.36	2.524	1.17	2.262	1.05	4.734 (3.734, 6.468)	2.19 (1.73, 2.99)
	L3	120	76.69	1.281 (1.110, 1.516)	1.67 (1.45, 1.98)	0.916	1.19	0.697	0.91	0.935	1.22	1.960 (1.562, 2.632)	2.56 (2.04, 3.43)
MPV [fL]	L1	120	7.65	0.089 (0.077, 0.106)	1.17 (1.01, 1.38)	0.000	0.00	0.020	0.27	0.042	0.55	0.101 (0.084, 0.126)	1.32 (1.10, 1.64)
	L2	120	7.49	0.103 (0.089, 0.122)	1.38 (1.19, 1.63)	0.039	0.52	0.045	0.60	0.058	0.77	0.133 (0.109, 0.170)	1.77 (1.45, 2.27)
	L3	120	7.36	0.173 (0.150, 0.205)	2.35 (2.04, 2.78)	0.028	0.39	0.000	0.00	0.043	0.58	0.180 (0.159, 0.209)	2.45 (2.16, 2.84)

Parameter [Units]	Control Level	N	Mean	Within-Run (Repeatability)		Between-Run		Between-Day		Between Laboratory (Site)		Total (Reproducibility)	
				SD (95% CI)	%CV (95% CI)	SD	%CV	SD	%CV	SD	%CV	SD (95% CI)	%CV (95% CI)
%NRBC [/100 WBC]	L2	120	18.30	0.931 (0.806, 1.101)	5.09 (4.41, 6.02)	0.250	1.37	0.000	0.00	1.185	6.48	1.528 (1.028, 2.958)	8.35 (5.62, 16.17)
	L3	120	8.84	1.011 (0.876, 1.196)	11.44 (9.91, 13.54)	0.266	3.01	0.000	0.00	0.427	4.83	1.129 (0.961, 1.370)	12.78 (10.87, 15.51)
#NRBC [10^3/µL]	L2	120	1.46	0.067 (0.058, 0.079)	4.59 (3.97, 5.43)	0.023	1.59	0.000	0.00	0.110	7.50	0.131 (0.084, 0.293)	8.94 (5.73, 20.02)
	L3	120	0.23	0.027 (0.023, 0.032)	11.62 (10.07, 13.75)	0.008	3.42	0.000	0.00	0.016	6.65	0.032 (0.026, 0.042)	13.82 (11.25, 17.93)
%NEUT [%]	L1	120	58.35	1.734 (1.502, 2.051)	2.97 (2.57, 3.52)	0.161	0.28	0.432	0.74	1.247	2.14	2.185 (1.689, 3.096)	3.74 (2.89, 5.31)
	L2	120	59.79	1.867 (1.617, 2.209)	3.12 (2.70, 3.69)	0.000	0.00	1.010	1.69	1.256	2.10	2.466 (1.948, 3.364)	4.13 (3.26, 5.63)
	L3	120	58.65	1.957 (1.695, 2.315)	3.34 (2.89, 3.95)	0.485	0.83	0.856	1.46	1.133	1.93	2.466 (2.004, 3.206)	4.20 (3.42, 5.47)
%LYMPH [%]	L1	120	39.37	1.667 (1.444, 1.972)	4.23 (3.67, 5.01)	0.000	0.00	0.266	0.68	1.280	3.25	2.119 (1.608, 3.107)	5.38 (4.08, 7.89)
	L2	120	37.32	1.798 (1.558, 2.127)	4.82 (4.17, 5.70)	0.000	0.00	1.078	2.89	1.252	3.35	2.442 (1.918, 3.362)	6.54 (5.14, 9.01)
	L3	120	37.47	1.997 (1.730, 2.363)	5.33 (4.62, 6.31)	0.000	0.00	0.721	1.93	1.088	2.90	2.386 (1.953, 3.069)	6.37 (5.21, 8.19)

Parameter [Units]	Control Level	N	Mean	Within-Run (Repeatability)		Between-Run		Between-Day		Between Laboratory (Site)		Total (Reproducibility)	
				SD (95% CI)	%CV (95% CI)	SD	%CV	SD	%CV	SD	%CV	SD (95% CI)	%CV (95% CI)
%MONO [%]	L1	120	2.02	0.584 (0.506, 0.691)	28.89 (25.02, 34.18)	0.000	0.00	0.000	0.00	0.227	11.21	0.626 (0.537, 0.752)	30.99 (26.55, 37.21)
	L2	120	2.45	0.663 (0.574, 0.784)	27.02 (23.41, 31.97)	0.167	6.80	0.096	3.90	0.279	11.39	0.744 (0.633, 0.903)	30.35 (25.82, 36.84)
	L3	120	3.12	0.761 (0.659, 0.900)	24.43 (21.16, 28.90)	0.093	2.99	0.181	5.80	0.244	7.85	0.825 (0.716, 0.972)	26.47 (22.99, 31.22)
%EO [%]	L1	120	0.17	0.141 (0.122, 0.167)	81.81 (70.86, 96.79)	0.040	23.27	0.061	35.50	0.085	49.39	0.180 (0.146, 0.237)	104.57 (84.48, 137.28)
	L2	120	0.31	0.191 (0.166, 0.226)	62.20 (53.88, 73.59)	0.076	24.60	0.062	20.21	0.110	35.63	0.241 (0.197, 0.311)	78.43 (64.12, 101.03)
	L3	120	0.68	0.351 (0.304, 0.415)	51.26 (44.40, 60.65)	0.000	0.00	0.078	11.41	0.247	36.13	0.436 (0.338, 0.614)	63.74 (49.43, 89.76)
%BASO [%]	L1	120	0.09	0.127 (0.110, 0.151)	136.58 (118.30, 161.59)	0.000	0.00	0.000	0.00	0.059	62.89	0.140 (0.118, 0.174)	150.36 (126.25, 185.94)
	L2	120	0.13	0.129 (0.112, 0.153)	102.85 (89.09, 121.68)	0.039	30.78	0.037	29.69	0.083	66.07	0.163 (0.130, 0.219)	129.51 (103.30, 173.66)
	L3	120	0.08	0.114 (0.099, 0.135)	139.61 (120.93, 165.18)	0.000	0.00	0.041	50.61	0.021	25.95	0.123 (0.108, 0.143)	150.75 (132.53, 174.84)
#NEUT [10^3/µL]	L1	120	9.87	0.307 (0.266, 0.363)	3.11 (2.69, 3.68)	0.052	0.52	0.103	1.04	0.090	0.92	0.340 (0.296, 0.400)	3.44 (3.00, 4.05)
	L2	120	4.78	0.191 (0.166, 0.226)	4.00 (3.47, 4.73)	0.040	0.84	0.091	1.90	0.073	1.54	0.228 (0.194, 0.276)	4.76 (4.06, 5.77)
	L3	120	1.55	0.098 (0.085, 0.116)	6.31 (5.47, 7.47)	0.000	0.00	0.058	3.76	0.035	2.28	0.119 (0.101, 0.145)	7.70 (6.54, 9.35)

Parameter [Units]	Control Level	N	Mean	Within-Run (Repeatability)		Between-Run		Between-Day		Between Laboratory (Site)		Total (Reproducibility)	
				SD (95% CI)	%CV (95% CI)	SD	%CV	SD	%CV	SD	%CV	SD (95% CI)	%CV (95% CI)
#LYMPH [10^3/µL]	L1	120	6.67	0.314 (0.272, 0.371)	4.71 (4.08, 5.57)	0.000	0.00	0.076	1.14	0.321	4.81	0.455 (0.322, 0.775)	6.83 (4.83, 11.62)
	L2	120	2.99	0.167 (0.144, 0.197)	5.58 (4.83, 6.60)	0.000	0.00	0.089	2.99	0.151	5.05	0.242 (0.179, 0.373)	8.10 (5.99, 12.47)
	L3	120	0.99	0.078 (0.067, 0.092)	7.85 (6.80, 9.29)	0.000	0.00	0.027	2.72	0.062	6.24	0.103 (0.078, 0.152)	10.39 (7.86, 15.33)
#MONO [10^3/µL]	L1	120	0.34	0.098 (0.085, 0.116)	28.72 (24.88, 33.98)	0.000	0.00	0.000	0.00	0.032	9.46	0.104 (0.090, 0.122)	30.24 (26.26, 35.64)
	L2	120	0.20	0.054 (0.047, 0.064)	27.46 (23.78, 32.49)	0.009	4.64	0.007	3.55	0.017	8.89	0.058 (0.050, 0.068)	29.45 (25.59, 34.68)
	L3	120	0.08	0.022 (0.019, 0.026)	26.57 (23.01, 31.43)	0.000	0.00	0.006	7.35	0.005	6.43	0.023 (0.020, 0.027)	28.30 (24.84, 32.91)
#EO [10^3/µL]	L1	120	0.03	0.023 (0.020, 0.028)	78.03 (67.59, 92.32)	0.007	22.07	0.011	35.94	0.013	42.81	0.029 (0.024, 0.038)	98.49 (80.80, 126.18)
	L2	120	0.02	0.015 (0.013, 0.018)	62.27 (53.94, 73.67)	0.007	28.12	0.005	22.02	0.008	35.11	0.019 (0.016, 0.025)	79.91 (65.61, 102.25)
	L3	120	0.02	0.010 (0.009, 0.012)	55.09 (47.72, 65.18)	0.000	0.00	0.002	10.14	0.006	35.78	0.012 (0.009, 0.016)	66.47 (52.47, 90.72)
#BASO [10^3/µL]	L1	120	0.02	0.021 (0.018, 0.024)	125.97 (109.11, 149.04)	0.005	28.13	0.000	0.00	0.010	59.59	0.023 (0.019, 0.029)	142.16 (119.16, 176.27)
	L2	120	0.01	0.010 (0.009, 0.012)	96.05 (83.20, 113.64)	0.004	34.14	0.003	25.88	0.006	61.24	0.013 (0.010, 0.017)	121.70 (97.41, 162.24)
	L3	120	0.00	0.004 (0.003, 0.004)	219.09 (189.77, 259.21)	0.000	0.00	0.001	52.44	0.001	70.12	0.004 (0.003, 0.005)	235.94 (204.89, 278.17)

Parameter [Units]	Control Level	N	Mean	Within-Run (Repeatability)		Between-Run		Between-Day		Between Laboratory (Site)		Total (Reproducibility)	
				SD (95% CI)	%CV (95% CI)	SD	%CV	SD	%CV	SD	%CV	SD (95% CI)	%CV (95% CI)
%RET [%]	L1	120	7.46	0.525 (0.455, 0.621)	7.03 (6.09, 8.32)	0.310	4.16	0.155	2.07	0.397	5.32	0.744 (0.583, 1.029)	9.97 (7.81, 13.79)
	L2	120	3.28	0.261 (0.226, 0.309)	7.97 (6.90, 9.43)	0.180	5.50	0.000	0.00	0.199	6.05	0.375 (0.295, 0.515)	11.42 (8.98, 15.69)
#RET [10^6/µL]	L1	120	0.19	0.014 (0.012, 0.017)	7.40 (6.41, 8.76)	0.008	4.06	0.004	2.09	0.010	4.99	0.019 (0.015, 0.026)	10.03 (8.02, 13.39)
	L2	120	0.14	0.012 (0.011, 0.014)	8.66 (7.50, 10.25)	0.006	4.41	0.005	3.23	0.010	7.01	0.017 (0.013, 0.025)	12.42 (9.55, 17.75)
HGB-RET [pg]	L1	120	25.22	0.320 (0.277, 0.379)	1.27 (1.10, 1.50)	0.213	0.84	0.000	0.00	0.327	1.30	0.504 (0.370, 0.794)	2.00 (1.47, 3.15)
	L2	120	26.11	0.369 (0.320, 0.437)	1.41 (1.23, 1.67)	0.146	0.56	0.149	0.57	0.362	1.39	0.557 (0.407, 0.883)	2.14 (1.56, 3.38)

5.1.5. Linearity

Linearity studies were conducted for WBC, RBC, HGB, HCT, PLT, and RET parameters. Serial dilutions of known high concentration of K_2 EDTA whole blood samples and whole blood components, which spanned the full measuring range for each of the aforementioned parameters, were run in both closed-tube mode and open-tube mode on multiple **cobas m** 511 systems. Each concentration from each dilution series was run for six (6) replicates [five (5) replicates for the reticulocyte series]. Results were analyzed in accordance with the CLSI EP06-A guideline. The method has been demonstrated to be linear from the lower limit to the upper limit and all results met acceptance criteria. Results for closed-tube mode are shown in Table 7. Open-tube mode results were comparable.

Table 7: Whole Blood Linearity

Parameter	Units	Intercept	Slope	Maximum Absolute Deviation (Relative)	Maximum Allowable Deviation (Relative)	Range
System 1						
WBC	$10^3/\mu L$	-0.040	1.022	0 (8%)	0.5 (15%)	(0.07, 404.8)
System 2						
WBC	$10^3/\mu L$	0.041	0.897	0.01 (11.3%)	0.5 (15%)	(0.04, 561.1)
System 3						
WBC	$10^3/\mu L$	0.011	0.984	0 (5%)	0.5 (15%)	(0.06, 460.5)
PLT	$10^3/\mu L$	-1.287	0.902	0.16 (6.9%)	20 (15%)	(9, 5000)
PLT	$10^3/\mu L$	-1.246	1.117	0.01 (4.1%)	20 (15%)	(5, 5020)
PLT	$10^3/\mu L$	0.374	0.963	N/A*	N/A*	(1, 5000)
PLT	$10^3/\mu L$	0.672	1.002	N/A*	N/A*	(0, 5130)
RET	%	0.010	0.789	0.01 (2.1%)	0.05 (20%)	(0.02, 0.63)
System 4						
RBC	$10^6/\mu L$	-0.072	0.990	0.03 (1.5%)	0.2 (10%)	(0.37, 8.26)
HGB	g/dL	-0.305	1.017	0.11 (1.1%)	0.5 (10%)	(1.1, 24.2)
HCT	%	-0.307	1.033	0.06 (2.4%)	1 (10%)	(3.2, 72.2)
PLT	$10^3/\mu L$	-2.149	0.884	0.03 (3.1%)	20 (15%)	(9, 5000)
RET	%	0.005	0.839	0 (5.5%)	0.05 (20%)	(0.03, 0.75)

Parameter	Units	Intercept	Slope	Maximum Absolute Deviation (Relative)	Maximum Allowable Deviation (Relative)	Range
System 5						
RBC	10^6/µL	-0.053	0.979	0.03 (2.2%)	0.2 (10%)	(0.37, 8.26)
HGB	g/dL	-0.199	1.016	0.1 (2.3%)	0.5 (10%)	(1.1, 24.2)
HCT	%	-0.329	1.019	0.1 (4.4%)	1 (10%)	(3.2, 72.2)
PLT	10^3/µL	-1.654	0.945	0.01 (1.8%)	20 (15%)	(9, 5000)
RET	%	0.000	0.616	N/A*	N/A*	(0.01, 0.75)
System 6						
RBC	10^6/µL	-0.045	0.971	N/A*	N/A*	(0.37, 8.26)
HGB	g/dL	-0.113	1.007	0.04 (0.6%)	0.5 (10%)	(1.1, 24.2)
HCT	%	-0.196	1.027	0.1 (2%)	1 (10%)	(3.2, 72.2)

*No deviation from linearity since the linear model was the best fit.

5.1.6. Carryover

Carryover was studied at each of the four (4) clinical sites for white and red blood cells and platelets consistent with the International Council for Standardization in Haematology (ICSH) guidelines for the evaluation of blood cell analyzers and CLSI H26-A2 standard. Samples with high percentages of blasts were also added to this evaluation, although not required by the ICSH guidelines or CLSI standard. In this evaluation, for each of the four (4) sample types, three (3) independent carryover experiments were conducted using residual high target value (HTV) whole blood samples. Filtered serum samples were used as low target value (LTV) samples. At each site and on each run day, HTV samples were run three (3) consecutive times immediately followed by three (3) LTV serum samples. Slides from the LTV serum samples were reviewed by an external hematopathologist to determine cell carryover from the HTV samples. Carryover results for the **cobas m** 511 system met acceptance criteria and are shown in Table 8.

Table 8: Summary of Carryover Results for All Sites Combined

Sample Type	Sample Size (N)	Mean Percent Carryover
White Blood Cells	12	0.000%
Red Blood Cells	12	0.000%
Platelets	12	0.001%
Blasts	12	0.000%

5.1.7. Interfering Substances

Studies were conducted to evaluate potential interference effects of hemolysis, lipemia and icterus (i.e., conjugated bilirubin and unconjugated bilirubin) and high concentrations of white blood cells (WBC) and platelets (PLT) on the **cobas m** 511 system. For hemolysis, lipemia and icterus, dose-response experiments were conducted using the ASSURANCE™ Interference Test Kit (Sun Diagnostics, New Gloucester, ME, USA) and whole blood donor samples. For the high concentrations of white blood cells and platelets, dose-response experiments were conducted using apheresis samples with matched whole blood from donors. Each interfering substance was tested in a series of six (6) incremental concentration samples. Results were analyzed using regression analysis in accordance with the CLSI EP07-A2 guideline. The results showed no significant interference effects of unconjugated bilirubin or conjugated bilirubin up to the maximum tested concentration of 40 mg/dL for each of the parameters that were evaluated. There were no significant hemolysis interference effects up to the maximum tested concentration of 1000 mg/dL for the parameters that were evaluated with the exception of clinically significant hemolysis interference effects observed at ≥ 672 mg/dL for HGB and ≥ 792 mg/dL for HCT. There were no significant lipemia interference effects up to the maximum tested concentration of 3000 mg/dL for the parameters that were evaluated with the exception that clinically significant lipemia interference effects were observed at ≥ 1646 mg/dL for WBC and ≥ 2459 mg/dL for #LYMPH. For all evaluated parameters, there were no significant interference effects of high concentrations of white blood cells up to the maximum tested concentration of 100.2 x 10^3/µL and high concentrations of platelets up to maximum tested concentration of 1166 x 10^3/µL.

5.1.8. Specimen Stability

A study of normal samples was conducted using thirty-one (31) whole blood samples from healthy volunteer donors. Samples were processed in duplicate at each of the following time points: baseline [time zero (0)] and after 9, 20, 26, 38, and 50 hours in both ambient (15ºC-25ºC) and refrigerated (2ºC-8ºC) storage conditions.

A study of the abnormal samples was conducted using fourteen (14) residual de-identified whole blood samples at targeted medical decision levels. Samples were processed in duplicate at each of the following time points: baseline [time zero (0)] and after 9, 26, and 50 hours in both ambient (15ºC-25ºC) and refrigerated (2ºC-8ºC) storage conditions.

The data from both normal and abnormal samples were combined in order to determine the extent of changes in all reported parameters over an extended period of time up to fifty (50) hours. Each parameter was analyzed separately at both ambient and refrigerated temperatures. For each time point, results were compared to the respective baseline [zero (0) hour] results. The combined results demonstrated stability for normal and abnormal samples up to or beyond twenty-four (24) hours.

5.1.9. Anticoagulant Comparison Study

Studies were conducted to demonstrate comparability between whole blood samples collected into K_2 and K_3 EDTA. Forty-four (44) whole blood samples from healthy volunteer donors and forty (40) residual whole blood samples that included thirty (30) targeted abnormal samples were evaluated. Samples from healthy donors were collected via venipuncture into separate K_2 and K_3 EDTA blood collection tubes as recommended in the CLSI H26-A2 standard. Each tube was processed on a single **cobas m** 511 system and the K_2 EDTA results compared to K_3 EDTA results for all reportable parameters. Residual whole blood samples collected into K_3 EDTA were processed on a **cobas m** 511 system and the predicate device. Results from the **cobas m** 511 system and the predicate device were compared for all reportable parameters. Correlation and bias were assessed in accordance with the CLSI EP09-A3 guideline. All acceptance criteria were met, demonstrating equivalency of results obtained from samples collected into K_2 EDTA and K_3 EDTA.

5.1.10. Venous and Capillary Blood Method Comparisons

Studies were conducted to demonstrate comparability between whole blood samples collected via venipuncture (venous) and finger-stick (capillary), as recommended in the CLSI H26-A2 standard. Forty (40) whole blood samples from healthy volunteer donors were utilized. Blood was drawn twice from each healthy donor, once via venipuncture and once via finger-stick. Additionally, forty (40) residual whole blood capillary samples, which included thirty (30) targeted abnormal samples, were evaluated in a method comparison analysis with the predicate device. All samples were processed in the open-tube mode on the predicate device and the **cobas m** 511 system. Results from the **cobas m** 511 system and the predicate device were compared for all reportable parameters. Correlation and bias were assessed in accordance with the CLSI EP09-A3 guideline. Overall, the data demonstrate comparable results between venous and capillary blood processed on the **cobas m** 511 system.

5.1.11. Mode to Mode Analysis

A study was conducted at the four (4) clinical sites to compare results from samples processed in the **cobas m** 511 system open-tube mode versus the closed-tube mode. For this study, samples processed in the closed-tube mode were automatically mixed on the **cobas m** 511 system, while samples processed in the open-tube mode were manually mixed prior to processing. Correlation and bias between the closed-tube and open-tube mode results were determined in accordance with the CLSI EP09-A3 guideline based on the results of either a Passing-Bablok or Deming regression model. For the %NRBC and #NRBC parameters the mean difference was used to calculate bias in accordance with the CLSI EP09-A3 guideline. The results were found to be acceptable in that all twenty-six (26) reportable parameters that were evaluated met acceptance criteria.

5.1.12. Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ)

A study was conducted to evaluate LoB, LoD and LoQ for the **cobas m** 511 system according to the CLSI EP17-A2 guideline. To determine LoB, testing was performed on three (3) individual test days using preserved RBC samples. The calculated LoB for WBC is 0.05 x 10^3/µL and for PLT is 1 x 10^3/µL. To determine LoD, residual whole blood samples with targeted low level values that were greater than the LoB were used. Testing was performed on three (3) individual

test days, using two (2) residual whole blood samples with targeted low level values for WBC and PLT parameters on each day. The calculated LoD for WBC is 0.08 x $10^3/\mu L$ and for PLT is 3 x $10^3/\mu L$. To determine LoQ, residual whole blood samples with targeted low level values that were greater than the LoD were required. Testing was performed on three (3) individual test days for WBC and PLT samples. The calculated LoQ for WBC is 0.24 x $10^3/\mu L$ and for PLT is 6 x $10^3/\mu L$.

5.1.13. Reference Intervals

Reference ranges from normal healthy donors were established for adult males, adult females, and the following six (6) pediatric subgroups: 0 to <6 months, 6 to <24 months, 2 to <6 years, 6 to <12 years, 12 to <18 years (female), and 12 to <18 years (male). For each targeted population, normal reference ranges for all parameters reported by the **cobas m** 511 system were calculated in accordance with the CLSI EP28-A3c guideline. Adult reference ranges were established using data from four (4) sites, while the pediatric data was established using data from a single site. The normal reference ranges for adult and pediatric cohorts are consistent with those in the published literature. Reference intervals may differ because of differences in sex, age, diet, fluid intake, or geographic location. Therefore, it is recommended that each laboratory establish its own expected reference intervals based upon their individual patient populations.

6. PROPOSED LABELING

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

7. CONCLUSIONS

The information provided in this Premarket Notification 510(k) supports a determination of substantial equivalence for the **cobas m** 511integrated hematology analyzer.