May 21, 2024

Horiba ABX Sas
Caroline Ferrer
Regulatory Affairs Manager
Parc Euromedecine, Rue du Caducee BP7290
Montpellier Cedex 4, 34184
France

Re: K232946
Trade/Device Name: Yumizen H2500
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated differential cell counter
Regulatory Class: Class II
Product Code: GKZ
Dated: September 14, 2023
Received: September 20, 2023

Dear Caroline Ferrer:

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 (the 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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Min Wu -S

Min Wu, Ph.D.
Branch Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K232946

Device Name
Yumizen H2500

Indications for Use *(Describe)*
The Yumizen H2500 is a quantitative multiparameter fully automated hematology analyzer intended for in-vitro diagnostic use in clinical laboratories by qualified healthcare professionals for the screening of patient populations.

The Yumizen H2500 is intended to perform tests on the following specimens:
• Anticoagulated whole blood specimens
• Body fluids (synovial fluids, serous fluids and cerebrospinal fluids).

The Yumizen H2500 classifies and enumerates the following parameters:
• A complete blood count (CBC) consisting of TNC, WBC, RBC, HGB, calculated HCT, MCV, calculated MCH, calculated MCHC, RDW-SD, RDW-CV, PLT, PLT-Ox, LPF, MPV.
• A leukocyte differential count consisting of LYM (%/#), MON (%/#), NEU (%/#), EOS (%/#), BAS (%/#), IMG (%/#)
• A nucleated red blood cell count consisting of NRBC (%/#).
• A reticulocyte analysis consisting of RET (%/#), calculated CRC, IRF, RHCC.
• Quantitative determination of blood cells in synovial fluids, serous fluids and cerebrospinal fluids consisting of BFWBC, BFRBC, BFPN (%/#), BFMN (%/#).

Note: Venous and capillary whole blood should be collected in K2EDTA anticoagulant. Serous and synovial fluids should be collected without anticoagulant or in K2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with cerebrospinal fluid specimens is neither required nor recommended. Alternatively, Sodium Heparin or Lithium Heparin may be used for synovial fluid.

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.

510(k) Safety and Effectiveness Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements 21 CFR 807.92 (b)(3).

Submitted by:
Company: HORIBA ABX SAS
Address:
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Date submitted: May 20th, 2024

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K232946

B. Applicant

HORIBA ABX SAS (Brand HORIBA Medical)

C. Proprietary and Established Names

Yumizen H2500

D. Regulatory Information

Product Code	Class	Regulation section	Regulation Description	Panel
GKZ	II	864.5220	Automated Differential Cell Counter	Hematology

II. Submission / Device Overview

A. Purpose for Submission

Clearance for a new device: Yumizen H2500

B. Parameters

TNC, WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW-SD, RDW-CV, PLT, MPV, LYM (%/#), MON (%/#), NEU (%/#), EOS (%/#), BAS (%/#), IMG (%/#), NRBC (%/#), BFWBC, BFRBC, BFPN (%/#), BFMN (%/#), PLT-Ox, LPF, RET (%/#), CRC, IRF, RHCC

C. Type of Test

A complete blood count (CBC)

A leukocyte differential count

A nucleated red blood cell count

A reticulocyte analysis

A body fluid count

III. Intended Use/Indications for Use

A. Intended Use(s)

See Indications for Use below.

B. Indications for Use

The Yumizen H2500 is a quantitative multiparameter fully automated hematology analyzer intended for in-vitro diagnostic use in clinical laboratories by qualified healthcare professionals for the screening of patient populations.

The Yumizen H2500 is intended to perform tests on the following specimens:

- Anticoagulated whole blood specimens
- Body fluids (synovial fluids, serous fluids and cerebrospinal fluids).

The Yumizen H2500 classifies and enumerates the following parameters:

- A complete blood count (CBC) consisting of TNC, WBC, RBC, HGB, calculated HCT, MCV, calculated MCH, calculated MCHC, RDW-SD, RDW-CV, PLT, PLT-Ox, LPF, MPV.
- A leukocyte differential count consisting of LYM (%/#), MON (%/#), NEU (%/#), EOS (%/#), BAS (%/#), IMG (%/#)
- A nucleated red blood cell count consisting of NRBC (%/#).
- A reticulocyte analysis consisting of RET (%/#), calculated CRC, IRF, RHCC.
- Quantitative determination of blood cells in synovial fluids, serous fluids and cerebrospinal fluids consisting of BFWBC, BFRBC, BFPN (%/#), BFMN (%/#).

Note: Venous and capillary whole blood should be collected in K2EDTA anticoagulant. Serous and synovial fluids should be collected without anticoagulant or in K2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with cerebrospinal fluid specimens is neither required nor recommended. Alternatively, Sodium Heparin or Lithium Heparin may be used for synovial fluid.

C. Special Conditions for Use Statement

Rx – For Prescription Use Only

IV. Device/System Characteristics

A. Device Description

The HORIBA Medical analyzer modules Yumizen H2500 are multi-parameter hematology analyzers intended to perform tests on whole blood samples collected in K2EDTA and body fluids (synovial and serous) collected in K2EDTA anticoagulant. The analyzers can also perform tests on cerebrospinal fluids which should not be collected in any anticoagulant.

The Analyzer Units (Yumizen H2500) aspirate, dilute, mix, and analyze blood and body fluid samples.
The Yumizen H2500 model provides Complete Blood Count (CBC), Differential (DIFF), Reticulocyte counts (RET) and Optical Platelet counts as well as Body Fluid counts (BF).

The analyzer models may function with:

- a Data Management Unit (Yumizen P8000) which is the interface with the laboratory connections (LIS) and the Analyzer Unit(s). Through its interface, the Yumizen P8000 enables the user to monitor the workflow of patient data, centralize result data, perform reflex testing, customize rules, centralize the validation operations, run quality control, manage quality assurance on results.

B. Principles of Operation

The HORIBA Yumizen H2500 uses impedance variation, optical and fluorescence flow cytometry, hydrodynamic focusing, and absorption spectrophotometry technologies to measure, count, and calculate hematological parameters in samples.

- Impedance variation consists in measuring the proportional signal response to the volume of the particle generated by its passage through a calibrated micro aperture concurrent with an electric current.
- Optical and fluorescence flow cytometry is a process used to count and measure the properties of cells or particles as they are carried by fluid through a sensing zone.
  The cells are counted with impedance variation technology and physical and chemical characteristics of cells or particles are measured via light absorbency response from a light beam, or fluorescence response from a laser.
  The Yumizen H2500 uses double hydrodynamic sequential system (DHSS) flow cytometry to focus and align cells into a single-file micro aperture through the sensing zone.
  Two cell-free liquid sheaths surround the diluted sample and move with it in a laminar flow. The laminar flow prevents any mixing between the two liquid sheaths and the diluted sample.
- Absorption spectrophotometry is based on the linear relationship between the amount of light that a well-mixed, nonflowing sample absorbs at a particular

absorption band and the concentration of an absorbing entity in the sample (Beer-Lambert Law).
To perform absorption spectrophotometry, the system uses the hemoglobin dilution as the sample and a specific reagent to release, oxidize and stabilize all heme iron from erythrocytes. The resulting complexes are quantified by spectrophotometry at a wavelength of 555nm.

Impedance variation technology through a calibrated micro aperture is used to analyse whole blood samples for RBC, PLT, TNC and body fluids samples (BFRBC).
Flow cytometry technology is used to:

- Separate NRBC from TNC to get the WBC and make the differential white blood cell formula with absorbency measurement.
- Analyse whole blood samples for RET with fluorescence measurement.
- Analyse whole blood samples for PLT with absorbency measurement (PLT-Ox)
- Analyse body fluids samples (BFWBC)

Absorption spectrophotometry is used to measure the HGB concentration.
All the other hematological parameters are calculated or derived from these different measurements.

Based on the available technologies and types of tests, the following analytical modes are available on the analyzers:

Table 1 - Analytical modes

Analytical Modes	**Corresponding tests**
CBC	Complete blood count
DIF	Complete blood count Leukocyte differential count
DIF_LV	Complete blood count Leukocyte differential count for low values
RBC_PLTO	Complete blood count PLT-Ox
RET	Reticulocyte analysis
CBR (CBC + RET)	Complete blood count and Reticulocyte analysis
DIR (DIF + RET)	Complete blood count Leukocyte differential count Reticulocyte analysis
CBF	Body fluid count

C. Instrument Description

a. Instrument Name:

Yumizen H2500

b. Specimen Identification:

Tube sample ID can be identified manually using an external keyboard or the virtual keyboard or automatically using the integrated barcode reader or an external barcode reader.

c. Specimen Sampling and Handling:

The **Yumizen H2500** operates in two sampling modes:

- Automatic sampling (auto mixer and auto loader)
- Manual sampling (STAT mode)

d. Calibration:

Calibration is a procedure that is performed during specific situations such as installation, maintenance or service intervention. It ensures that the precision and accuracy of the analyzer are acceptable, so that accurate measurements are performed by the analyzer.
Calibration is performed using materials with assigned values that are traceable to standard reference methods. It is recommended that the laboratory calibrate using ABX Minocal, which is a commercial whole blood calibrator.

e. Quality Control:

Quality control allows the user to monitor a set of analyses based on known sample values and ranges over a period of several months. Statistical computation performed on these populations allows the extraction of qualitative information related to the stability of the instrument.
The manufacturer's instructions are to be followed for material and frequency of quality control analysis.
Commercial controls:
ABX Difftrol, for CBC and Differential parameters
ABX Minotrol Retic, for Retic parameters
BFTROL, for Body Fluid parameters

V. Substantial Equivalence Information

A. Predicate Device Name(s)

Sysmex XN-series

B. Predicate 510(k) Number(s)

K112605

C. Comparison with Predicate

Table 2 - Comparison with predicate

Device & Predicate Device(s)		**K112605**
Device Trade Name	**Yumizen H2500**	**Sysmex® XN-Series (XN-10, XN-20) Automated Hematology Analyzers (K112605)**
General Device Characteristics Similarities		
Regulation	21 CFR 864.5220	21 CFR 864.5220
Product code	GKZ	GKZ
Intended Use/Indications for use	The Yumizen H2500 is a quantitative multiparameter fully automated hematology analyzer intended for in-vitro diagnostic use in clinical laboratories by qualified healthcare professionals for the screening of patient populations. The Yumizen H2500 is intended to perform tests on the following specimens: • Anticoagulated whole blood specimens • Body fluids (synovial fluids, serous fluids and cerebrospinal fluids). The Yumizen H2500 classifies and enumerates the following parameters: • A complete blood count (CBC) consisting of TNC, WBC, RBC, HGB, calculated HCT, MCV, calculated MCH, calculated MCHC, RDW-SD, RDW-CV, PLT, PLT-Ox, LPF, MPV. • A leukocyte differential count consisting of LYM (%/#), MON (%/#), NEU (%/#), EOS (%/#), BAS (%/#), IMG (%/#) • A nucleated red blood cell count consisting of NRBC (%/#). • A reticulocyte analysis consisting of RET (%/#), calculated CRC, IRF, RHCC. • Quantitative determination of blood cells in synovial fluids, serous fluids and cerebrospinal fluids consisting of BFWBC, BFRBC, BFPN (%/#), BFMN	The Sysmex® XN-10 and XN-20 modules 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 for whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT (PLT-I, PLT-F), NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, NRBC%/#, IG%/#, RDW-CV, RDW-SD, MPV, RET%/#, IRF, IPF, 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 fluids (CSF), serous fluids (peritoneal, pleural) and synovial fluids. Whole blood should be collected in K2 or K3EDTA anticoagulant and, Serous and Synovial fluids in K2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with CSF specimens is neither required nor recommended.

Device & Predicate Device(s)		**K112605**
Device Trade Name	**Yumizen H2500**	**Sysmex® XN-Series (XN-10, XN-20) Automated Hematology Analyzers (K112605)**
	(%/#). Note: Venous and capillary whole blood should be collected in K2EDTA anticoagulant. Serous and synovial fluids should be collected without anticoagulant or in K2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with cerebrospinal fluid specimens is neither required nor recommended. Alternatively, Sodium Heparin or Lithium Heparin may be used for synovial fluid.	
Test Principle (same)	Performs hematology analyses according to the Double Hydrodynamic Sequential System, flow cytometry method (using a semiconductor laser and fluorescent dyes)	Performs hematology analyses according to the Hydro Dynamic Focusing (DC Detection), flow cytometry method (using a semiconductor laser and fluorescent dyes)
Test parameters* (same)	WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEU%/#, LYM%/#, MON%/#, EOS%/#, BAS%/#, NRBC%/#, RDW-CV, RDW-SD, MPV, RET%/#, IRF, IMG%/#, BFWBC, BFRBC, BFMN%/#, BFPMN%/#	WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT (PLT-I), NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, NRBC%/#, RDW-CV, RDW-SD, MPV, RET%/#, IRF, IG%/#, WBC-BF, RBC-BF, MN%/#, PMN%/#
Specimen types	Whole blood Body fluid	Whole blood Body fluid
Use of Controls/Calibrators	Yes	Yes
Modes of Operation	Automatic Rack mode Body Fluid Analysis Mode Manual mode (both close and open cap) (Sample placed in tube holder position) Low Value mode (DIF_LV)	Sampler Analysis Mode Body Fluid Analysis Mode Manual Closed Analysis Mode Manual Open Cap Analysis Mode (Sample placed in tube holder position) Low WBC Mode (LWBC)
Type of tubes	Venous and capillary tubes	Venous and capillary tubes
Patient population	Adult and Pediatric	General Patient population
Instrument operating temperature	15 to 30°C	15 to 30°C
Relative humidity	Up to 85%	30 to 85%
Transportation condition	From -20°C (-4°F) to +60°C (+140°F).	-10 to 60°C

* Different names/formats of equivalent parameters are used between the Yumizen H2500 device and Sysmex® XN-series; therefore, equivalent parameters are listed in the same order.

Device & Predicate Device(s)		**K112605**
Device Trade Name	**Yumizen H2500**	**Sysmex® XN-Series (XN-10, XN-20) Automated Hematology Analyzers (K112605)**
General Device Characteristics – Differences		
Test Principle (different)	HGB: Spectrophotometry using cyanide-free lysis	HGB: Spectrophotometry using SLS-hemoglobin method
Test parameters (different)	Whole blood parameters: PLT-Ox, LPF, RHCC, CRC Body Fluid parameters: /	Whole blood parameters: PLT-F, IPF, RETHe# Body Fluid parameters: TC-BF
Reagents	ABX DILUENT 10L (Diluent) ABX DILUENT 20L (Diluent) ABX LYSEBIO 1L (Lyse) ABX BASOLYSE 5L (Lyse) NUCEDIFF 1L (Lyse) ABX FLUOCYTE 0.5L (Stain) ABX CLEANER 1L (Cleaner) ABX MINOCLAIR 0.5L (Cleaner)	CELLPACKTM DCL (Diluent) CELLPACKTM DFL (Diluent) LYSERCELL WNR (Lyse) LYSERCELL WDF (Lyse) LYSERCELL WPC (Lyse) SULFOLYSER (Lyse) FLUOROCELL WNR (Stain) FLUOROCELL WDF (Stain) FLUOROCELL RET (Stain) FLUOROCELL PLT (Stain) FLUOROCELL WPC (Stain)
Controls / Calibrators	Whole Blood: ABX DIFFTROL (3 Levels) ABX MINOTROL RETIC (3 Levels) ABX MINOCAL Body Fluid: BFTROL (2 Levels)	Whole Blood: XN-Check - 3 Levels XN CAL (XN-10/X-20 Calibrator) XN CAL PF (Platelet F Calibrator) Body Fluid: XN Check BF – 2 Levels
Modes of Operation	No-predilute analysis mode No dilution of sample	Pre-dilute Analysis Mode Dilute sample 1 :7
Throughput	Whole Blood: 120 samples/hour maximum depending on mode used. Body Fluid 20 samples/hour maximum	Whole Blood 100 samples/hour maximum depending on mode used. Body Fluid 40 samples/hour maximum
Sample Aspiration Volume	Rack analysis: 110 µL Manual analysis: 110 µL	Sampler Mode – 88 µL Manual (Closed Cap) Mode – 88 µL Manual (Open Cap) Mode – 88 µL Dilution Mode – 70 µL Body Fluid Mode – 88 µL
Dimension	870(W) x 730(H) x 670(D) mm	645(W) x 855(H) x 755(D) mm
Weight	about 99 kg	about 78 kg (including the sampler)

VI. Standards/Guidance Documents Referenced

Table 3 - List of standards

Standard reference	Standard Title [FDA recognition number]
CLSI EP05-A3	Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition [7-251]
CLSI EP06-A2	Evaluation of the Linearity of Quantitative Measurement Procedures [7-306]
CLSI EP07-A3	Interference Testing in Clinical Chemistry [7-275]
CLSI EP09-A3c	Measurement Procedure Comparison and Bias Estimation Using Patient Samples [7-296]
CLSI EP17-A2	Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition [7-233]
CLSI EP28-A3c	Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition [7-224]
CLSI EP37-A	Supplemental Tables for Interference Testing in Clinical Chemistry [7-284]
CLSI H20-A2	Reference Leukocyte (WBC) Differential Count (Proportional) and Evaluation of Instrumental Methods; Approved Standard - Second Edition [7-165]
CLSI H26-A2	Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Proposed Standard - Second Edition [7-210]
CLSI H44-A2	Methods for Reticulocyte counting (Automated blood cell counters, Flow cytometry, and Supravital dyes); Approved Guideline – Second edition
CLSI H56-A	Body Fluid Analysis for Cellular Composition; Approved Guideline. [7-163]
IEC 61010-1:2010+A1	Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements [19-34]
UL 61010-1:2012 R7.19	Standard for Safety for Electrical Equipment For Measurement, Control and Laboratory Use; Part 1: General Requirements [19-41]
IEC 60601-1-2: 2014	Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests [19-8]
IEC 60825-1: 2014	Safety of laser products - Part 1: Equipment classification, and requirements
IEC 62304: 2015	Medical device software - Software life cycle processes [13-79]
ISO 14971: 2019	Medical devices - Application of risk management to medical devices [5-125]
ISO 15223-1: 2021	Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements [5-134]

Standard reference	Standard Title [FDA recognition number]
ISO 18113-3: 2022	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 3: In vitro diagnostic instruments for professional use

VII. Performance Characteristics (if/when applicable)

A. Analytical Performance

a. Precision/Reproducibility:

Repeatability – Whole Blood

Repeatability studies were performed according to CLSI H26-A2 guide recommendations at four (4) test sites with seven (7) instruments using DIF, DIR, DIF_LV, or RBC_PLTO modes.
Within-run repeatability studies were performed using a total of 116 residual K2EDTA whole blood samples around medical decision levels and within the laboratory reference range. Contrived samples were utilized to cover the extremes of the analytical measuring range of some parameters.
Each sample was measured 12 consecutive times.
For each parameter, the mean and coefficient of variation (CV) were computed. All components of variation that were calculated met the pre-defined acceptance criteria. The results are summarized below.

Table 4 - Repeatability – Whole Blood normal samples

Target Range	Recommended Target Values	Parameter	N	Result Range	Max %CV	Max SD
Normal	4-10 10^9/L	WBC	37	4.27-9.84	2	0.150
Normal	4-10 10^9/L	TNC	36	4.27-9.84	1.8	0.150
Normal	3.6-6.2 10^{12}/L	RBC	58	3.66-5.92	1.5	0.057
Normal	12.0-18.0 g/dL	HGB	44	12.0-17.6	0.6	0.096
Normal	36-54 %	HCT	46	36.4-53.6	1.2	0.5
Normal	80-100 fL	MCV	87	80.4-99.4	0.5	0.530
Normal	27-32 pg	MCH	79	27.1-31.8	1.2	0.344
Normal	320-360 g/L	MCHC	84	320-355	1.2	3.954
Normal	5-17 %	RDWcv	71	12.6-16.9	2.7	0.350
Normal	10-49 fL	RDWsd	53	31.4-48.9	3.4	1.453
Normal	150-500 10^9/L	PLT	64	156-479	5	11.595
Normal	8-12 fL	MPV	83	8.2-12	3	0.242
Normal	150-500 10^9/L	PLT-Ox	16	155-469	4.7	12.317
Normal	2-12 %	LPF	15	2.1-11.2	20.7	0.834
Normal	25-50 %	LYM%	26	25.5-43.2	3.8	1.101
Normal	2-10 %	MON%	41	3.8-9.7	9.1	0.845
Normal	45-80 %	NEU%	36	46.8-79.2	1.9	1.093
Normal	0.5-5 %	EOS%	38	0.5-4.9	18.2	0.442
Normal	0-2.5 %	BAS%	75	0-2.2	39.3	0.370

Target Range	Recommended Target Values	Parameter	N	Result Range	Max %CV	Max SD
Normal	0.5-3 %	IMG%	46	0.5-2.8	19.4	0.355
Normal	0.8-5 10^9/L	LYM#	48	0.84-4.25	7.2	0.129
Normal	0.1-1 10^9/L	MON#	42	0.33-0.98	9.1	0.058
Normal	2 - 8 10^9/L	NEU#	36	2.18-7.32	2.6	0.113
Normal	0-0.5 10^9/L	EOS#	44	0.02-0.48	22	0.027
Normal	0-0.25 10^9/L	BAS#	73	0.00-0.21	38.4	0.053
Normal	0-0.2 10^9/L	IMG#	48	0.01-0.19	11.6	0.039
Normal	0-2.5 %	NRBC%	59	0.00-2.18	18.8	0.481
Normal	0-0.15 10^9/L	NRBC#	54	0.00-0.02	0.0	0.017
Normal	0.5-3 %	RET%	33	0.52-2.94	11.6	0.209
Normal	20-150 10^9/L	RET#	35	28-147	17.1	12.525
Normal	0.75-3 %	CRC	32	0.83-2.93	12.2	0.249
Normal	0.15-0.3	IRF	17	0.15-0.29	14.4	0.033
Normal	27-35 pg	RHCc	21	28.41-34.86	3.5	1.077

Table 5 - Repeatability – Whole Blood abnormal samples

Target Range	Recommended Target Values	Parameter	N	Result Range	Max %CV	Max SD
Low	0.1-2 10^9/L	WBC	1	0.81	3.9	0.032
Low	2-4 10^9/L	WBC	4	2.81-3.97	1.8	0.065
Low	0.5-4 10^9/L	TNC	5	0.81-3.97	3.9	0.065
Low	0.3-3.0 10^{12}/L	RBC	25	1.17-2.99	1.7	0.038
Low	3.0-3.6 10^{12}/L	RBC	23	3.02-3.56	0.9	0.028
Low	4.0 – 8.0 g/dL	HGB	18	4.1-7.9	1.0	0.098
Low	8.0-12.0 g/dL	HGB	43	8.0-11.8	0.9	0.121
Low	4-36 %	HCT	59	9.8-35.6	1.6	0.4
Low	40-80 fL	MCV	14	59.6-80.0	0.4	0.322
Low	30 -150 10^9/L	PLT	9	56-130	8	7.236
Low	30 -150 10^9/L	PLT-Ox	2	106-131	4.6	4.830
Low	10 - 25%	LYM%	20	10.9-24.4	6	0.889
Low	20 - 45%	NEU%	6	26.7-43.5	3.7	0.981
Low	0.00 - 0.15	IRF	18	0.03-0.15	25.6	0.031
High	10-30 10^9/L	WBC	31	10.03-19.9	1.9	0.330
High	30-300 10^9/L	WBC	5	34.4-150.73	1	0.966
High	10-300 10^9/L	TNC	41	10.01-153.24	3.6	5.540
High	6.2-8 10^{12}/L	RBC	10	6.43-7.83	0.7	0.045

Target Range	Recommended Target Values	Parameter	N	Result Range	Max %CV	Max SD
High	18.0-24.0 g/dL	HGB	9	19.0-22.0	0.4	0.134
High	54-67 %	HCT	10	54.1-65.7	0.8	0.5
High	100-200 fL	MCV	13	101.7-137.7	0.5	0.531
High	17-50 %	RDWcv	13	17.1-28.6	2.9	0.644
High	49-100 fL	RDWsd	31	49.4-82.8	2.8	2.317
High	500-2500 10^9/L	PLT	18	515-959	2	13.968
High	500-2500 10^9/L	PLT-Ox	10	678-1047	2.3	23.649
High	12-100 %	LPF	2	15.2-15.4	5.3	0.811
High	50-100	LYM%	2	54.6-58.8	1.3	0.735
High	10-100	MON%	15	10.1-20.5	5.6	0.903
High	80-100	NEU%	1	84.5-84.5	0.5	0.447
High	5-100	EOS%	5	6.4-22.7	4.9	0.770
High	2.5-100	BAS%	2	3.4-6	11.4	0.458
High	3-100	IMG%	7	3.6-26.8	16.1	1.272
High	5-30010^9/L	LYM#	2	5.2-6.85	2.6	0.136
High	1-300 10^9/L	MON#	13	1.04-6.15	6	0.297
High	8-300 10^9/L	NEU#	5	8.02-13.94	1.9	0.266
High	0.5-300 10^9/L	EOS#	5	0.51-2.3	5.6	0.064
High	0.25-300 10^9/L	BAS#	2	0.33-2.22	8	0.091
High	0.2-300 10^9/L	IMG#	18	0.2-22.92	19.1	1.145
High	2.5-100	NRBC%	10	4.0-45.9	8.1	2.827
High	0.15-20 10^9/L	NRBC#	14	0.16-6.03	17	0.414
High	3 - 35 %	RET%	7	3.3-11.1	7.4	0.286
High	150-1200 10^9/L	RET#	5	160-301	4.8	0.008
High	3 - 35 %	CRC	5	3.2-6.7	4.7	0.235
High	0.3-1	IRF	4	0.31-0.39	8.3	0.026
High	35-100 pg	RHCc	8	35.2-45.2	2.9	1.055

Repeatability – Body Fluid

Repeatability studies were performed according to CLSI H56-A guide recommendations at four (4) test sites with seven (7) instruments using CBF mode.
Within-run repeatability studies were performed using a total of 87 residual body fluid samples (Synovial, Serous and Cerebrospinal Fluids) around medical decision levels and

within the laboratory reference range. Contrived samples were utilized to cover the extremes of the analytical measuring range of some parameters.
Each sample was measured 4 to 10 consecutive times.
For each parameter, the mean and coefficient of variation (CV) were computed. The data supports the validity of the repeatability performance claims for the instrument models tested, as summarized in Table below.

Table 6 - Repeatability – Body Fluid serous samples

Target Range	Recommended Target Values	Parameter	N	Result Range	Max %CV	Max SD
Level 1	5-100 10^6/L	BFWBC	8	0-29	10.4	8.5
Level 1	1500-5000 10^6/L	BFRBC	5	0-7597	17	500.8
Level 1	5-100 10^6/L	BFPN#	21	0-97	36.6	4.4
Level 1	5-25	BFPN%	21	0-7	39.7	3.6
Level 1	5-300v10^6/L	BFMN#	21	0-54	9.2	5.9
Level 1	5-80	BFMN%	14	0-4	11.7	3.6
Level 2	100-600 10^6/L	BFWBC	18	101-492	13.6	28.8
Level 2	5000-5000000 10^6/L	BFRBC	21	8445-775828	9.4	7596.8
Level 2	100-10000 10^6/L	BFPN#	11	110-3316	8.1	96.7
Level 2	25-100	BFPN%	8	25-85	15.4	6.7
Level 2	300-10000 10^6/L	BFMN#	17	322-2554	7.8	53.8
Level 2	80-100	BFMN%	24	81-99	4.4	3.7
Level 3	600-10000 10^6/L	BFWBC	12	699-3887	4.4	111.2

Table 7 - Repeatability – Body Fluid synovial samples

Target Range	Recommended Target Values	Parameter	N	Result Range	Max %CV	Max SD
Level 1	5-100 10^6/L	BFWBC	7	19-82	11.8	9.7
Level 1	1500-5000 10^6/L	BFRBC	2	1864-3440	18.1	482.2
Level 1	5-100 10^6/L	BFPN#	8	6-63	37.6	6.3
Level 1	5-25	BFPN%	6	8-24	20.3	3.4
Level 1	5-300 10^6/L	BFMN#	11	9-236	20.6	7.7
Level 1	5-80	BFMN%	17	13-79	17.6	3.6
Level 2	100-600 10^6/L	BFWBC	7	110-520	10.5	23.2
Level 2	5000-5000000 10^6/L	BFRBC	16	5084-3798731	8.7	30369.5
Level 2	100-10000 10^6/L	BFPN#	12	103-6179	8.8	213.2
Level 2	25-100	BFPN%	15	34-87	9.8	5.4
Level 2	300-10000 10^6/L	BFMN#	11	484-6700	14.4	604.4
Level 2	80-100	BFMN%	5	83-93	6.6	5.6
Level 3	600-10000 10^6/L	BFWBC	13	1144-9540	4.8	222.0

Table 8 - Repeatability – Body Fluid CSF samples

Target Range	Recommended Target Values	Parameter	N	Result Range	Max %CV	Max SD
Level 1	5-100 10^6/L	BFWBC	9	17-89	19.2	8.6
Level 1	1500-5000 10^6/L	BFRBC	3	2080-3678	16.0	357.2
Level 1	5-100 10^6/L	BFPN#	1	18	16.2	2.9
Level 1	5-25	BFPN%	2	6-8	0.0	0.0
Level 1	5-300 10^6/L	BFMN#	9	11-209	27.5	5.6
Level 1	5-80	BFMN%	4	5-45	18.2	3.5
Level 2	100-600 10^6/L	BFWBC	3	260-546	10.0	54.8
Level 2	5000-5000000 10^6/L	BFRBC	7	8555-2887945	7.0	11989.8
Level 2	100-10000 10^6/L	BFPN#	6	144-2929	14.7	65.8
Level 2	25-100	BFPN%	6	55-99	17.7	10.8
Level 2	300-10000 10^6/L	BFMN#	1	4387-4387	1.5	66.1
Level 2	80-100	BFMN%	4	84-97	9.3	7.8
Level 3	600-10000 10^6/L	BFWBC	3	640-4657	2.3	69.2

Reproducibility – Whole Blood

Reproducibility studies were performed to evaluate the within-run, between-run, between-day, between-instrument, and total precision of the Yumizen H2500 analyzer. Testing was performed using three (3) levels of each whole blood control material (ABX Difftrol and ABX Minotrol Retic). Each level was run in duplicate twice each day for a minimum of 20 days using a single calibration and reagent lot at each of the four (4) test sites. The results were analyzed in accordance with the CLSI EP05-A3 approved guideline and met the acceptance criteria. Results are summarized below.

Table 9 - Reproducibility ABX Difftrol – combined sites analysis

Parameter	Level	N	Mean	Within run		Between run		Between day		Between site[(a)]		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
WBC 10^9/L	L	320	2.28	0.04	1.60	0.01	0.35	0.00	0.00	0.07	3.22	0.08	3.62
	N	320	7.28	0.06	0.83	0.06	0.80	0.00	0.00	0.19	2.66	0.21	2.90
	H	320	18.22	0.13	0.69	0.08	0.45	0.11	0.60	0.49	2.70	0.53	2.88
RBC 10^{12}/L	L	320	2.41	0.02	0.78	0.01	0.34	0.00	0.00	0.02	0.64	0.03	1.07
	N	320	4.82	0.03	0.66	0.00	0.00	0.01	0.12	0.01	0.18	0.03	0.69
	H	320	5.54	0.04	0.76	0.00	0.00	0.01	0.20	0.04	0.63	0.06	1.01
HGB g/dL	L	320	6.141	0.025	0.40	0.18	0.29	0.00	0.00	0.55	0.89	0.63	1.02
	N	320	13.679	0.041	0.30	0.000	0.00	0.022	0.16	0.113	0.83	0.122	0.89
	H	320	17.086	0.049	0.29	0.030	0.18	0.020	0.12	0.131	0.77	0144	0.84
HCT %	L	320	18.61	0.15	0.80	0.10	0.52	0.05	0.27	0.29	1.57	0.35	1.86
	N	320	41.02	0.31	0.74	0.08	0.19	0.08	0.20	0.56	1.35	0.92	1.57
	H	320	51.44	0.42	0.82	0.00	0.00	0.16	0.30	0.80	1.56	0.90	1.78
MCV fL	L	320	77.08	0.23	0.30	0.21	0.27	0.27	0.35	0.80	1.04	0.90	1.17
	N	320	85.18	0.24	0.28	0.16	0.19	0.22	0.26	1.06	1.24	1.12	1.32
	H	320	92.82	0.28	0.30	0.16	0.17	0.28	0.30	1.15	1.24	1.22	1.32
MCH pg	L	320	25.42	0.21	0.84	0.10	0.41	0.00	0.00	0.38	1.48	0.44	1.75
	N	320	28.40	0.19	0.68	0.03	0.09	0.00	0.00	0.26	0.91	0.32	1.14
	H	320	30.83	0.23	0.75	0.00	0.00	0.08	0.25	0.35	1.12	0.42	1.37
MCHC g/L	L	320	329.87	2.74	0.83	2.05	0.62	0.85	0.26	8.23	2.50	8.96	2.72
	N	320	333.50	2.54	0.76	0.76	0.23	0.57	0.17	7.17	2.15	7.66	2.30
	H	320	332.25	2.60	0.78	0.00	0.00	1.28	0.39	7.61	2.29	8.14	2.45
RDW-CV %	L	320	15.93	0.25	1.57	0.05	0.33	0.04	0.23	0.29	1.83	0.39	2.45
	N	320	13.59	0.20	1.50	0.02	0.12	0.13	0.97	0.30	2.20	0.39	2.84
	H	320	12.34	0.20	1.58	0.10	0.82	0.09	0.73	0.27	2.16	0.36	2.90
RDW-SD fL	L	320	42.15	0.96	2.29	0.23	0.54	0.36	0.85	1.07	2.54	1.50	3.57
	N	320	39.79	0.78	1.96	0.33	0.83	0.61	1.54	0.93	2.34	1.40	3.51
	H	320	40.40	0.79	1.97	0.44	1.09	0.62	1.54	0.92	2.28	1.44	3.56
PLT 10^9/L	L	320	63.07	3.36	5.32	0.00	0.00	1.00	1.58	0.92	1.46	3.62	5.74
	N	320	247.03	6.45	2.61	0.00	0.00	1.61	0.65	7.27	2.95	9.86	3.99
	H	320	483.15	8.15	1.69	2.53	0.52	0.00	0.00	14.94	3.09	17.21	3.56
PLT-Ox 10^9/L	L	320	65.02	5.63	8.66	1.72	2.65	2.68	4.12	3.46	5.32	7.34	11.28
	N	320	244.78	6.79	2.77	2.49	1.02	3.56	1.45	6.30	2.58	10.23	4.18
	H	320	478.70	10.77	2.25	0.00	0.00	3.77	0.79	8.28	1.73	14.09	2.94
MPV fL	L	320	11.17	0.17	1.53	0.06	0.54	0.04	0.39	0.07	0.59	0.20	1.77
	N	320	10.66	0.09	0.81	0.03	0.32	0.03	0.27	0.10	0.96	0.14	1.32
	H	320	10.44	0.06	0.60	0.05	0.47	0.00	0.00	0.11	1.02	0.13	1.27
LPF	L	320	2.20	0.68	30.91	0.00	0.00	0.37	17.05	0.33	14.93	0.84	38.33

Parameter	Level	N	Mean	Within run		Between run		Between day		Between site[(a)]		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
%	N	320	1.54	0.31	19.91	0.08	5.44	0.25	16.31	0.31	19.91	0.51	32.99
	H	320	1.36	0.21	15.38	0.09	6.45	0.17	12.51	0.25	18.09	0.37	27.61
LYM# 10^9/L	L	320	0.40	0.02	4.39	0.01	1.53	0.00	0.00	0.01	3.34	0.02	5.72
	N	320	1.33	0.03	2.16	0.01	0.83	0.00	0.00	0.04	3.10	0.05	3.87
	H	320	1.60	0.04	2.48	0.01	0.51	0.02	1.30	0.06	3.47	0.07	4.49
LYM%	L	320	17.52	0.85	4.83	0.00	0.00	0.16	0.89	0.20	1.12	0.88	5.04
	N	320	18.30	0.38	2.09	0.13	0.72	0.00	0.00	0.11	0.60	0.42	2.29
	H	320	8.80	0.23	2.57	0.07	0.76	0.02	0.26	0.07	0.78	0.25	2.81
MON# 10^9/L	L	320	0.15	0.01	9.16	0.01	6.08	0.00	0.00	0.01	3.89	0.02	11.67
	N	320	0.49	0.02	4.94	0.01	2.31	0.00	0.00	0.02	3.81	0.03	6.65
	H	320	0.82	0.04	5.28	0.03	3.39	0.00	0.00	0.04	4.87	0.07	7.95
MON%	L	320	6.67	0.60	9.05	0.41	6.13	0.00	0.00	0.18	2.76	0.75	11.28
	N	320	6.77	0.33	4.88	0.20	2.89	0.00	0.00	0.12	1.74	0.40	5.93
	H	320	4.49	0.23	5.16	0.16	3.63	0.00	0.00	0.17	3.81	0.33	7.37
NEU# 10^9/L	L	320	1.43	0.04	2.65	0.00	0.00	0.01	0.69	0.05	3.32	0.06	4.30
	N	320	4.67	0.06	1.21	0.05	1.12	0.00	0.00	0.12	2.52	0.14	3.02
	H	320	13.49	0.12	0.87	0.06	0.47	0.07	0.54	0.36	2.64	0.39	2.87
NEU%	L	320	62.91	0.99	1.57	0.49	0.77	0.23	0.37	0.00	0.00	1.13	1.79
	N	320	64.14	0.49	0.77	0.25	0.39	0.00	0.00	0.20	0.31	0.59	0.92
	H	320	74.06	0.36	0.48	0.09	0.12	0.00	0.00	0.19	0.25	0.41	0.56
EOS# 10^9/L	L	320	0.12	0.01	9.62	0.00	3.54	0.01	5.80	0.00	3.33	0.01	12.24
	N	320	0.23	0.02	8.04	0.01	2.33	0.00	0.00	0.00	1.28	0.02	8.47
	H	320	0.72	0.04	5.61	0.01	1.94	0.01	1.98	0.01	1.63	0.05	6.47
EOS%	L	320	5.28	0.49	9.36	0.18	3.34	0.29	5.58	0.18	3.42	0.63	11.90
	N	320	3.10	0.25	8.00	0.06	2.03	0.00	0.00	0.07	2.34	0.27	8.57
	H	320	3.93	0.23	5.73	0.04	0.98	0.05	1.39	0.05	1.19	0.24	6.10
BAS# 10^9/L	L	320	0.10	0.00	3.37	0.00	1.37	0.00	1.03	0.00	4.86	0.01	6.16
	N	320	0.32	0.00	1.46	0.00	1.02	0.00	0.77	0.01	4.00	0.01	4.45
	H	320	0.84	0.01	1.09	0.00	0.00	0.00	0.59	0.03	3.23	0.03	3.46
BAS%	L	320	4.37	0.06	1.44	0.03	0.70	0.05	1.19	0.10	2.19	0.13	2.97
	N	320	4.37	0.05	1.05	0.02	0.39	0.04	0.84	0.08	1.84	0.10	2.32
	H	320	4.58	0.04	0.82	0.00	0.00	0.01	0.25	0.03	0.76	0.05	1.15
NRBC# 10^9/L	L	320	0.17	0.01	4.63	0.00	1.75	0.00	0.00	0.01	3.32	0.01	5.96
	N	320	0.57	0.01	2.22	0.00	0.75	0.00	0.00	0.02	3.08	0.02	3.87
	H	320	0.69	0.02	2.48	0.00	0.70	0.01	1.28	0.02	3.47	0.03	4.51
NRBC%	L	320	7.50	0.36	4.84	0.00	0.00	0.07	0.99	0.08	1.12	0.38	5.06
	N	320	7.84	0.16	2.07	0.06	0.71	0.00	0.00	0.05	0.60	0.18	2.27
	H	320	3.77	0.10	2.75	0.00	0.00	0.00	0.00	0.03	0.70	0.11	2.84
IMG# 10^9/L	L	320	0.07	0.00	5.69	0.00	1.42	0.00	0.00	0.00	3.88	0.01	7.03
	N	320	0.24	0.00	1.65	0.00	1.22	0.00	0.09	0.01	2.48	0.01	3.22
	H	320	0.75	0.01	1.07	0.00	0.41	0.00	0.42	0.02	2.65	0.02	2.92
IMG%	L	320	3.25	0.08	2.51	0.04	1.15	0.00	0.00	0.01	0.41	0.09	2.79
	N	320	3.32	0.04	1.32	0.02	0.75	0.00	0.00	0.02	0.50	0.05	1.59
	H	320	4.14	0.04	1.08	0.00	0.03	0.00	0.00	0.02	0.54	0.05	1.21
TNC 10^9/L	L	320	2.45	0.04	1.49	0.01	0.49	0.00	0.00	0.08	3.20	0.09	3.57
	N	320	7.85	0.07	0.83	0.06	0.78	0.00	0.00	0.21	2.69	0.23	2.92
	H	320	18.91	0.13	0.68	0.08	0.44	0.12	0.63	0.52	2.73	0.55	2.91

(a) Control materials (ABX Difftrol, ABX Minotrol Retic and BFTROL) were analyzed at four sites using four instruments (one instrument per site). Between site analysis corresponds to between instrument analysis.

Table 10 - Reproducibility ABX Minotrol Retic – combined sites analysis

Parameter	Level	N	Mean	Within run		Between run		Between day		Between site[(a)]		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
RET# 10^9/L	1	320	65.31	4.40	6.73	1.63	2.50	0.30	0.45	2.20	3.36	5.19	7.94
	2	320	180.31	6.26	3.47	2.70	1.50	1.34	0.74	0.85	0.47	7.00	3.88
	3	320	355.78	8.31	2.34	3.59	1.01	2.92	0.82	0.75	0.21	9.54	2.68
RET%	1	320	1.86	0.12	6.69	0.05	2.45	0.00	0.00	0.07	3.60	0.15	7.99
	2	320	5.14	0.17	3.40	0.07	1.40	0.04	0.85	0.04	0.69	0.20	3.84
	3	320	10.04	0.23	2.31	0.10	0.95	0.07	0.68	0.04	0.39	0.26	2.62
CRC [%]	1	320	1.18	0.08	6.72	0.03	2.54	0.01	0.45	0.05	3.90	0.10	8.19
	2	320	3.21	0.11	3.47	0.05	1.49	0.03	0.94	0.05	1.55	0.13	4.19
	3	320	6.23	0.15	2.34	0.06	0.98	0.05	0.85	0.10	1.55	0.19	3.09
IRF	1	320	0.31	0.02	7.70	0.01	4.09	0.00	0.00	0.01	2.15	0.03	8.98
	2	320	0.48	0.01	3.12	0.01	2.11	0.00	0.00	0.03	5.61	0.03	6.75
	3	320	0.53	0.01	1.74	0.01	2.26	0.00	0.00	0.03	5.70	0.03	6.37
RBC 10^{12}/L	1	320	3.51	0.03	0.75	0.01	0.25	0.00	0.00	0.01	0.28	0.03	0.84
	2	320	3.51	0.02	0.63	0.01	0.42	0.00	0.00	0.01	0.39	0.03	0.85
	3	320	3.54	0.02	0.61	0.01	0.21	0.01	0.15	0.01	0.36	0.03	0.76
RHCC pg	1	320	23.66	0.58	2.44	0.29	1.22	0.24	1.03	0.24	1.03	0.73	3.09
	2	320	17.01	0.36	2.11	0.25	1.47	0.12	0.72	0.21	1.21	0.50	2.93
	3	320	12.52	0.30	2.44	0.26	2.06	0.14	1.13	0.21	1.71	0.47	3.79

(a) Control materials (ABX Difftrol, ABX Minotrol Retic and BFTROL) were analyzed at four sites using four instruments (one instrument per site). Between site analysis corresponds to between instrument analysis.

Reproducibility – Body Fluids

Reproducibility studies were performed to evaluate the within-run, between-run, between-day, between-instrument, and total precision of the Yumizen H2500 analyzer. Testing was performed using two (2) levels of the body fluid control material (BFTROL). Each level was run in duplicate twice each day for a minimum of 20 days using a single calibration and reagent lot at each of the four (4) test sites. The results were analyzed in accordance with the CLSI EP05-A3 approved guideline and met the acceptance criteria. Results are summarized below.

Table 11 - Reproducibility BFTROL – combined sites analysis

Parameter	Level	N	Mean	Within run		Between run		Between day		Between site[(a)]		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
BFRBC	2	320	77783	3258.20	4.19	0.00	0.00	0.00	0.00	2297.83	2.95	3986.96	5.13
	3	320	522119	10520.51	2.01	816.66	0.16	1142.11	0.22	15093.99	2.89	18452.13	3.55
BFWBC	2	320	227	7.93	3.50	4.87	2.15	0.00	0.00	10.97	4.84	14.39	6.34
	3	320	917	16.62	1.81	5.57	0.61	7.78	0.85	32.66	3.57	37.87	4.14
BFMN#	2	320	67	5.25	7.83	0.62	0.93	1.39	2.07	2.69	4.01	6.09	9.09
	3	320	155	7.76	4.99	0.00	0.00	1.76	1.13	4.36	2.81	9.07	5.84
BFMN%	2	320	30	2.09	7.05	0.00	0.00	0.47	1.58	0.18	0.60	2.15	7.25
	3	320	17	0.86	5.06	0.00	0.00	0.12	0.72	0.18	1.07	0.89	5.18

Parameter	Level	N	Mean	Within run		Between run		Between day		Between site[(a)]		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
BFPN#	2	320	160	7.35	4.60	3.26	2.04	0.00	0.00	8.24	5.16	11.51	7.21
	3	320	761	16.14	2.12	7.48	0.98	5.69	0.75	28.45	3.75	34.04	4.48
BFPN%	2	320	70	2.09	2.96	0.00	0.00	0.47	0.66	0.18	0.25	2.15	3.05
	3	320	83	0.86	1.03	0.00	0.00	0.12	0.15	0.18	0.22	0.89	1.06

(a) Control materials (ABX Difftrol, ABX Minotrol Retic and BFTROL) were analyzed at four sites using four instruments (one instrument per site). Between site analysis corresponds to between instrument analysis.

b. Linearity:

Linearity – Whole Blood

The study was performed according to CLSI EP06-A2 guide recommendations at one test site, using two (2) instruments:

- For CBC parameters: two (2) Yumizen H2500 with one different reagent lot on each instrument.
- For RET and PLT-Ox parameters, two (2) Yumizen H2500 with one different reagent lot on each instrument

For each parameter, the linearity range (commercial or prepared from dilutions of samples) using a minimum of seven (7) concentration levels was analyzed:

- One (1) sample underneath the lower limit of the linearity interval
- At least five (5) samples with concentrations over the entire linearity range
- One (1) sample over the upper limit of the linearity interval

Each level is tested in a minimum of four (4) replicates on two (2) instruments using two (2) reagent lots.
Results are presented in the table below. All results met the predefined acceptance criteria and were determined to be acceptable.

Table 12 - Whole Blood linearity summary

Parameter	Unit	Linearity range
WBC	10^9/L (10^3/µL)	0.06 – 344.50
TNC	10^9/L (10^3/µL)	0.06 – 344.50
RBC	10^{12}/L (10^6/µL)	0.17-8.63
HGB	g/dL	0.5 – 25.8
HCT	%	1.5 – 72.7
PLT	10^9/L (10^3/µL)	5 – 2706
PLT-Ox	10^9/L (10^3/µL)	7 – 2570
RET#	10^9/L	8 – 1276
NRBC#	10^9/L	0.00 – 21.21

Linearity – Body Fluids

The study was performed according to CLSI EP06-A2 guide recommendations at one test site, using two (2) instruments, with one different reagent lot on each instrument.

For each parameter, the linearity range (prepared from dilutions of samples) using a minimum of seven (7) concentration levels was analyzed:

- One (1) sample underneath the lower limit of the linearity interval
- At least five (5) samples with concentrations over the entire linearity range
- One (1) sample over the upper limit of the linearity interval

Each level is tested in a minimum of four (4) replicates on two (2) instruments using two (2) reagent lots.
Results are presented in the table below. All results met the predefined acceptance criteria and were determined to be acceptable.

Table 13 - Body Fluid linearity summary

Parameters	Unit	Linearity range
BFWBC	10^6/L	3 – 11 345
BFRBC	10^6/L	1079 – 5 394 633

c. Analytical Specificity/Interference:

Interferences – Whole Blood

The susceptibility of the Yumizen H2500 device to interference in the presence of hemoglobin, triglycerides, bilirubin, cholesterol, elevated WBCs, elevated RBCs, elevated PLTs, microcytic RBCs and other potential interferents was tested in whole blood samples collected in K2EDTA tubes, at four (4) test sites.

Hemoglobin, Lipemia, Bilirubin, Glucose and Yeast

For the Hemoglobin, Lipemia, Bilirubin, Glucose and Yeast studies, interferent levels were tested with samples at two concentration levels, according to CLSI EP7-A3 guidelines.
The potential interfering substance is added to a sample and the bias relative to a control portion of the sample is evaluated ("paired-difference testing"). This bias was compared to the acceptance criteria.

The following parameters were evaluated for each potential interferent:

Table 14 - Whole Blood Parameters - Potential Interferents

Parameters	Potential interferent
WBC, HGB, LYM#, MON#, NEU#, EOS#, RET#	Hemoglobin
WBC, LYM#, MON#, NEU#, EOS#, HGB, PLT, PLT-Ox	Lipemia (Triglycerides or Cholesterol)
HGB, PLT, PLT-Ox, MPV	Bilirubin (Total and Direct)
MCV	Glucose
PLT, PLT-Ox, MPV	Yeast

The Yumizen H2500 device were considered not susceptible to interference from Hemoglobin, Lipemia, Bilirubin, Glucose and Yeast, if the absolute difference or % difference criteria were met for each measurand.

Whole Blood Intrinsic Interferences

A study was conducted to evaluate the susceptibility of the Yumizen H2500 device to interference from Intrinsic Interferences in native whole blood specimens, according to CLSI H26-A2 guidelines.

This study utilized a subset of samples tested in the method comparison study, in four (4) test sites, where unique, native whole blood specimens collected in K2EDTA tubes were identified with potential interferents for interference analysis. A minimum of 17 specimens were evaluated per interferent.

The Yumizen H2500 device results for a parameter were considered not susceptible to interference from an interferent condition if the visual inspection of the difference plot does not differentiate the two groups (with and without interferent). The visual inspection was used for this analysis because the study compares the Yumizen H2500 device and another method (Sysmex XN-10) in specimens with the interfering condition. Overall, the Yumizen H2500 device demonstrated no interference in measuring WBC, RBC, PLT, MCV, and HGB from elevated WBC, RBC, and PLT measurands in native whole blood specimens.

Table 15 - Potential interferent study summary

Interferent	Level	Conclusion
Hemoglobin	1.4 g/dL	No interference was detected on WBC, HGB, Differential and RET parameters.
Lipemia	Cholesterol 453.6 mg/dL and/or Triglycerides 2621.7 mg/dL	No significant effect was detected on WBC and Differential, HGB, MCH, MCHC, PLT, PLT-Ox and MPV parameters.
Total Bilirubin	60 mg/dL	No interference was detected with total bilirubin on HGB, MCH, MCHC, PLT, PLT-Ox, MPV parameters.
Direct Bilirubin (Conjugated)	19 mg/dL	Conjugated bilirubin has a significant effect on low HGB level (4 g/dL). No interference was detected with conjugated bilirubin on MCH, MCHC, PLT,

Interferent	Level	Conclusion
		PLT-Ox, MPV parameters.
Glucose	960 mg/dL	No interference detected on MCV, RDW-CV and RDW-SD parameters.
Yeast (Saccharomyces boulardii)	50 mg/L	No interference was detected on PLT, PLT-Ox, MPV parameters.
Leukocytosis (Elevated WBCs)	>32 10^9/L WBC	Significant effect on low MCV
	>59 10^9/L WBC	Significant effect on high MCV
	300 10^9/L	No interference detected on RBC, HGB, MCH, MCHC, RDW-CV, RDW-SD, PLT, PLT-Ox, MPV and NRBC parameters.
Fragile WBC	-	No interference was detected.
Thrombocytosis (Elevated Platelets)	PLT>600 10^9/L	No interference detected on WBC, WBC Differential, RBC, HGB, HCT, MCV, RDW-CV, RDW-SD, MPV parameters.
Macrothrombocytosis	-	PLT-Ox and LYM# potentially increased. No interference detected on WBC/WBC differential, RBC, HGB, HCT, MCV, MCH, MCHC, RDW-CV, RDW-SD, PLT, MPV, NRBC, RET parameters.
Platelet Aggregates	-	PLT, PLT-Ox and LYM# potentially impacted. No interference was detected on WBC/WBC differential, MPV, NRBC and RET.
Dual RBC population	-	RDW-SD potentially impacted. No interference detected on RBC, HCT, MCV, MCH, MCHC, RDW-CV parameters.
RBC abnormal morphology	-	MCV, RDW-SD, PLT-Ox and MPV potentially impacted. No interference detected on RBC, HGB, HCT, RDW-CV and RET parameters.
RBC Fragments (schiztocytes)	-	PLT-Ox and RET potentially impacted. No interference detected on PLT, MPV and RET parameters.
RBC inclusions	-	PLT-Ox potentially impacted. No interference detected on RBC, HCT, MCV, MCH, MCHC, RDW-CV parameters.
RBC Microcytosis	MCV<75 fL	PLT, MPV and RET potentially impacted. No interference was detected on RBC and PLT-Ox parameters.
Erythroblasts	NRBC%>10%	WBC and Differential potentially impacted. No interference detected on RET parameter.

Interferences - Body Fluids

The susceptibility of the Yumizen H2500 device to interference in the presence of hemoglobin, triglycerides, bilirubin, total protein, mesothelial cells, malignant cells, and other interferents was tested in body fluid samples collected in K2EDTA tubes, at four (4) test sites.

Hemoglobin, Lipemia, Bilirubin, Total Protein and Yeast

For the Hemoglobin, Lipemia, Bilirubin, Total Protein and Yeast studies, interferent levels were tested with samples at two concentration levels, according to CLSI EP7-A3 guidelines.
The potential interfering substance is added to a sample and the bias relative to a control portion of the sample is evaluated ("paired-difference testing"). This bias was compared to the acceptance criteria.

The following parameters were evaluated for each potential interferent:

Table 16 - Whole Blood Parameters - Potential Interferents

Parameters	Potential interferent
BFWBC, BFRBC	Hemoglobin
BFWBC, BFRBC	Lipemia (Triglycerides)
BFWBC, BFRBC	Bilirubin (Total and Direct)
BFWBC, BFRBC	Total protein
BFWBC	Yeast

The Yumizen H2500 device were considered not susceptible to interference from Hemoglobin, Lipemia, Bilirubin and Total Protein, if the absolute difference or % difference criteria were met for each measurand.
Interference from yeast was detected.

Body Fluid Intrinsic Interferences

A study was conducted to evaluate the susceptibility of the Yumizen H2500 device to interference from Intrinsic Interferences in native body fluid specimens, according to CLSI H26-A2 guidelines.
This study utilized a subset of samples tested in the method comparison study, in four (4) test sites, where unique, native body fluid specimens were identified with potential interferents for interference analysis.

The Yumizen H2500 device results for a parameter were considered not susceptible to interference from an interferent condition if the visual inspection of the difference plot does not differentiate the two groups (with and without interferent). The visual inspection was used for this analysis because the study compares the Yumizen H2500 device and another method (Sysmex XN-10) in specimens with the interfering condition. Overall, the Yumizen H2500 device demonstrated no interference in measuring BFWBC and BFRBC from presence of mesothelial cells or malignant cells in native body fluid specimens.

Interferences from the presence of crystals or liposomal particles on BFWBC is well described in literature.

Table 17 - Potential interferent study summary

Interferent	Level	Conclusion
Hemoglobin	2 g/dL	No significant effect was detected on BFWBC, BFRBC on three (3) types of body fluids.
Lipemia	Triglycerides 1593 mg/dL	No significant effect was detected on BFWBC, BFRBC on serous fluids.
Total Bilirubin	25.9 mg/dL	No significant effect was detected on BFWBC, BFRBC on serous fluids.
Direct Bilirubin (Conjugated)	39.3 mg/dL	No significant effect was detected on BFWBC, BFRBC on serous fluids.
Total Protein	50 mg/L	No interference detected on BFWBC, BFRBC parameters on all three (3) types of body fluids.
Yeast (Saccharomyces boulardii)	50 mg/dL	Significant effect was detected on BFWBC on all three (3) types of body fluids..
Crystals	-	This interference is known and documented in bibliography: crystals may interfere with BFWBC and generate a pollution on the scattergram.
Mesothelial cells	-	No interference detected with mesothelial cells on native serous fluids.
Malignant cells	-	No interference detected with mesothelial cells on native serous and CSF fluids.
Liposomal particles	-	This interference is known and documented in bibliography: liposomal particles may interfere with BFWBC and generate a pollution on the scattergram.

d. Traceability, Stability, Expected Values:

Stability - Whole Blood samples:

A total of 14 whole venous blood specimens (collected in K2EDTA) were analyzed on the Yumizen H2500 at three (3) test sites. Following the collection (T0), each specimen was divided in half, with one sample stored at ambient temperature (20-24ºC) and the other stored under refrigerated conditions (2-8ºC). Testing for stability was performed at regular intervals after (T0). When sufficient volume is available, each time point is tested in duplicate.
Acceptance criteria for each parameter was established for defined time intervals at each storage condition as the difference between the recovery of the parameter at defined time points and time point zero (T0). The acceptance criteria were met for each claimed storage conditions:

Table 18 - Whole Blood - Sample stability study results

	Room temperature	**Refrigerated temperature**
WHOLE BLOOD	24h for CBC/LMNE/NRBC/ RET parameters	48h for CBC/LMNE/NRBC parameters 72h for RET parameters

Stability - Body Fluid samples:

28 body fluid specimens (13 serous, 7 synovial, and 8 cerebrospinal fluids) were analyzed on the analyzer at two (2) test sites. Following the collection (T0), each specimen was stored at ambient temperature (20-24ºC). For serous and synovial fluids, testing for stability was performed at 6, 24 and 27 hours after (T0), and for cerebrospinal fluids, testing for stability was performed at three (3), four (4) and 4.5 hours after (T0).
The acceptance criteria for sample stability is given as an acceptable maximum bias of the value at T with the value at (T0).

Table 19 – Body Fluid - Sample stability study results

	Room temperature
Serous fluids	24h for BFWBC/BFRBC/BFPN/BFMN parameters
Synovial fluids	24h for BFWBC/BFRBC/BFPN/BFMN parameters
CSF	4h for BFWBC/BFRBC/BFPN/BFMN parameters

Per established literature, body fluid samples should be stored at room temperature and analyzed within 1 hour of collection.

e. Detection Limits:

Limit of Blank - Whole Blood

The Limit of Blank (LoB) for WBC, TNC, RBC, HGB, HCT, PLT, PLT-Ox and RET# was determined according to CLSI EP17-A2 guide recommendations. Testing was conducted over a minimum of five (5) days using six (6) blank samples, with two (2) different reagent lots on different analyzers, each sample being run 10 repeated times. The results obtained from all samples were used to calculate the LoB for each parameter.

Limit of Detection - Whole Blood

The Limit of Detection (LoD) for WBC, TNC, RBC, HGB, HCT, PLT, PLT-Ox and RET# was determined according to CLSI EP17-A2 guide recommendations. Testing was conducted over a minimum of three (3) days using six (6) low concentration whole blood samples, with two (2) different reagent lots on different analyzers, each sample being run 10 repeated times. The results obtained from all samples were used to calculate the LoD for each parameter.

Limit of Quantitation - Whole Blood

The Limit of Quantitation (LoQ) for WBC, TNC, RBC, HGB, HCT, PLT, PLT-Ox, RET# and RET% was determined according to CLSI EP17-A2 guide recommendations. Testing was conducted over a minimum of three (3) days using at least four (4) low concentration whole blood samples, with two (2) different reagent lots on different analyzers, each sample being run 10 repeated times. The results obtained from all samples were used to calculate the Mean, Total error, and LoQ for each parameter. All results met the predefined acceptance criteria and were determined to be acceptable.

Table 20 - Whole Blood - Analytical Sensitivity Summary

Parameter	Unit	LoB	LoD	LoQ
WBC	**10^9/L (10^3/µL)**	0.05	0.07	0.10
TNC	**10^9/L (10^3/µL)**	0.05	0.07	0.10
RBC	**10^{12}/L (10^6/µL)**	0.01	0.05	0.20
HGB	**g/dL**	0.1	0.3	0.8
HCT	**%**	0.1	0.3	2
PLT	**10^9/L (10^3/µL)**	2	4	7
PLT-Ox	**10^9/L (10^3/µL)**	2	6	10
RET#	**10^9/L (10^3/µL)**	2	7	10

*: Not applicable, ratio result

Limit of Blank - Body Fluid

The Limit of Blank (LoB) for BFWBC and BFRBC was determined according to CLSI EP17-A2 guide recommendations. Testing was conducted over a minimum of five (5) days using six (6) blank samples, with two (2) different reagent lots on different analyzers, each sample being run 10 repeated times. The results obtained from all samples were used to calculate the LoB for each parameter.

Limit of Detection - Body Fluid

The Limit of Detection (LoD) for BFWBC and BFRBC was determined according to CLSI EP17-A2 guide recommendations. Testing was conducted over a minimum of three (3) days using six (6) low concentration body fluid samples, with two (2) different reagent lots on different analyzers, each sample being run 10 repeated times. The results obtained from all samples were used to calculate the LoD for each parameter.

Limit of Quantitation - Body Fluid

The Limit of Quantitation (LoQ) for BFWBC and BFRBC was determined according to CLSI EP17-A2 guide recommendations. Testing was conducted over a minimum of three (3) days using at least four (4) low concentration body fluid samples, with two (2) different reagent lots on different analyzers, each sample being run 10 repeated times. The results obtained from all samples were used to calculate the Mean, Total error, and LoQ for each parameter. All results met the predefined acceptance criteria and were determined to be acceptable.

Table 21 - Body Fluids - Analytical Sensitivity Summary

Parameter Unit	LoB	LoD	LoQ
BFWBC 10^6/L	2	4	5
BFRBC 10^6/L	500	1000	1500

f. Assay Cut-Off:

Not applicable

g. Accuracy (Instrument):

Not applicable

h. Carry-over:

Carry-over - Whole Blood

Carryover was evaluated by assaying whole blood K2EDTA samples with high WBC, RBC, HGB, PLT, PLT-Ox, RET% and RET# counts three consecutive times (high 1, high 2, high 3) followed immediately by testing samples with low target values consecutively three times (low 4, low 5, low 6) in accordance with CLSI H26-A2 guide. Three sets of carry-over sequences were run for each parameter on three analyzers at one (1) test site.

The percentage of carryover is calculated using the formula below:

$$Ct\ \% = \frac{low\ 4 - low\ 6}{high\ 3 - low\ 6} \times 100$$

Where:

low 4: is the first low sample analyzed after the high sample runs
low 6: is the last low sample analyzed after the high sample runs
high 3: is the last high sample analyzed

All carry-over results are within specifications for the Yumizen H2500 systems.

Carry-over – Body Fluids

Carryover was evaluated by assaying body fluid samples (serous and synovials) with high BFWBC and BFRBC counts three consecutive times (high 1, high 2, high 3) followed immediately by testing samples with low target values consecutively three times (low 4, low 5, low 6) in accordance with CLSI H26-A2 guide. Three sets of carry-over sequences were run for each parameter on three analyzers at one (1) test site.

The percentage of carryover is calculated using the formula below:

$$Ct\ \% = \frac{low\ 4 - low\ 6}{high\ 3 - low\ 6} \times 100$$

Where:

low 4: is the first low sample analyzed after the high sample runs
low 6: is the last low sample analyzed after the high sample runs
high 3: is the last high sample analyzed

All carry-over results are within specifications for the Yumizen H2500 systems.

B. Comparison Studies

a. Method Comparison with Predicate Device:

Method comparison studies were conducted to assess the performance of the Yumizen H2500 device, compared to the predicate device (Sysmex XN-Series, XN-10, K112605), according to EP9-A3 guidelines.

Whole Blood

A method comparison study was conducted to assess the performance of the Yumizen H2500 device when compared to the predicate device, Sysmex XN-Series (XN-10, XN-20) (K112605). A total of 969 venous and/or capillary specimens collected in K2EDTA from pediatric (≤21 years) and adult subjects including a wide variety of disease states (clinical conditions) were tested across four (4) clinical sites (two (2) US sites and two (2) European sites).

Venous and/or capillary whole blood leftover specimens were collected in K2EDTA tubes from a wide range of demographics (age and sex) and disease states (clinical conditions). In total, there were 143 specimens collected from subjects with one or more known medical conditions. Study sites aimed to cover the target assay reportable range for the parameters. A maximum of 10% samples were permitted to be contrived to cover the entire target assay reportable range.

Each specimen was tested within six (6) hours from the time of collection in two (2) replicates on the Yumizen H2500 and one (1) replicate on the Sysmex XN-10 System, when sufficient volume was available. Specimens were tested on the Yumizen H2500 and the Sysmex XN-Series (XN-10, XN-20) within three (3) hours of each other.

A Passing-Bablok regression analysis was performed. Bias at medical decision points were also evaluated for all sites combined. All results were within the predefined acceptance criteria and found to be acceptable. Overall, the Yumizen H2500 demonstrated comparable performance to the predicate device, Sysmex XN-Series (XN-10, XN-20) (K112605) in an intended use population in a clinical laboratory setting.

A summary of the results is presented in the table below:

Table 22 - Whole Blood method comparison data summary

Parameter (unit)	N	Sample Range	r (95% CI)	Slope (95% CI)	Intercept (95% CI)
WBC (10^9/L) (10^3/µL)	936	0.19 - 232	0.996 [0.996;0.997]	1.012 [1.007 ; 1.017]	0.045 [0.014 ; 0.076]
TNC (10^9/L) (10^3/µL)	937	0.19 - 232	0.996 [0.996;0.997]	1.006 [1.00 ; 1.01]	0.080 [0.05 ; 0.11]
RBC (10^{12}/L) (10^6/µL)	941	0.54 - 7.31	0.997 [0.997;0.998]	1.006 [1.00 ; 1.01]	-0.017 [-0.03 ; 0.01]
HGB (g/dL)	941	2 - 22.1	0.998 [0.998;0.998]	1.000 [1 ; 1]	0.000 [0 ; 0]
HCT (%)	941	5.8 - 65.3	0.985 [0.983;0.987]	1.036 [1.024 ; 1.048]	-1.4 [-1.9 ; -1.0]
MCV (fL)	940	60.6 - 140	0.893 [0.88;0.906]	1.015 [0.983 ; 1.052]	-2.119 [-5.381 ; 0.804]
MCH (pg)	940	18.6 - 46.1	0.976 [0.973;0.979]	1.000 [1.000 ; 1.022]	0.000 [-0.662 ; 0.000]
MCHC (g/L)	940	278 - 379	0.184 [0.106;0.238]	0.545 [0.5 ; 0.6]	149.500 [132.0 ; 164.5]
RDW-CV (%)	924	10.7 - 30.4	0.872 [0.857;0.888]	0.868 [0.833 ; 0.901]	2.316 [1.860 ; 2.843]
RDW-SD (fL)	932	28.2 - 112	0.834 [0.815;0.854]	1.161 [1.111 ; 1.219]	-7.946 [-10.370 ; -5.495]
PLT (10^9/L) (10^3/µL)	939	9 - 1780	0.995 [0.995;0.996]	0.977 [0.970 ; 0.984]	2.841 [1.447 ; 3.996]
PLT-Ox (10^9/L) (10^3/µL)	801	10 - 1780	0.988 [0.986;0.99]	0.962 [0.949 ; 0.974]	3.570 [1.503 ; 5.583]
LPF (%)	791	0.4 - 40.9	0.872 [0.856;0.889]	0.833 [0.786 ; 0.888]	0.067 [-0.100 ; 0.222]
MPV (fL)	877	7.2 - 13.3	0.901 [0.888;0.913]	1.000 [0.976 ; 1.000]	-1.000 [-1.000 ; -0.763]
NRBC% (%)	930	0 - 66.7	0.927 [0.918;0.936]	0.609 [0.455 ; 0.73]	0.000 [0.000 ; 0.000]
NRBC# (10^9/L) (10^3/µL)	930	0.00 – 9.08	0.951 [0.945;0.957]	0.636 [0.466 ; 0.736]	0.000 [0.000 ; 0.000]

Parameter (unit)	N	Sample Range	r (95% CI)	Slope (95% CI)	Intercept (95% CI)
LYM% (%)	821	0.7 - 99.2	0.985 [0.983;0.987]	0.990 [0.984 ; 0.996]	0.685 [0.501 ; 0.875]
LYM# (10^9/L) (10^3/µL)	821	0.05 – 204.00	0.993 [0.993;0.994]	1.005 [0.995 ; 1.015]	0.064 [0.047 ; 0.080]
MON% (%)	843	0.1 - 87.9	0.938 [0.93;0.946]	1.008 [1.000 ; 1.042]	0.402 [0.122 ; 0.600]
MON# (10^9/L) (10^3/µL)	843	0.00 - 98.90	0.955 [0.949;0.961]	1.128 [1.102 ; 1.152]	-0.028 [-0.041 ; -0.015]
NEU% (%)	834	0.2 - 95.6	0.984 [0.982;0.986]	0.988 [0.982 ; 0.995]	0.373 [-0.051 ; 0.769]
NEU# (10^9/L) (10^3/µL)	834	0.0 - 75.3	0.968 [0.964;0.972]	1.014 [1.008 ; 1.021]	0.013 [-0.006 ; 0.031]
EOS% (%)	928	0.0 - 78.1	0.984 [0.982;0.986]	0.918 [0.902 ; 0.933]	0.345 [0.310 ; 0.385]
EOS# (10^9/L) (10^3/µL)	928	0.00 - 23.30	0.976 [0.973;0.979]	1.000 [0.984 ; 1.000]	0.020 [0.020 ; 0.021]
BAS# (10^9/L) (10^3/µL)	897	0.00 - 12.30	0.902 [0.89;0.914]	1.000 [0.818 ; 1.000]	-0.010 [-0.010 ; -0.006]
BAS% (%)	897	0.0 - 13.1	0.712 [0.679;0.744]	1.000 [0.931 ; 1.0]	-0.200 [-0.200 ; -0.1]
IMG% (%)	834	0 - 37	0.867 [0.85;0.884]	0.733 [0.674 ; 0.778]	0.080 [0.050 ; 0.129]
IMG# (10^9/L) (10^3/µL)	834	0.00 - 72.40	0.982 [0.979;0.984]	0.854 [0.802 ; 0.901]	0.001 [-0.002 ; 0.002]
RET% (%)	919	0.31 - 20.20	0.901 [0.888;0.913]	1.020 [0.997 ; 1.045]	-0.140 [-0.182 ; -0.100]
RET# (10^9/L) (10^3/µL)	914	10 - 565	0.925 [0.916;0.934]	0.997 [0.968 ; 1.026]	-3.355 [-5.626 ; -1.907]
CRC (%)	919	0.1 - 12.7	0.939 [0.931;0.947]	0.986 [0.961 ; 1.012]	-0.067 [-0.099 ; -0.034]
IRF	914	0.00 - 0.54	0.778 [0.752;0.803]	0.833 [0.807 ; 0.868]	0.023 [0.017 ; 0.028]
RHCC (pg)	913	12.7 - 49.1	0.654 [0.616;0.69]	1.226 [1.159 ; 1.294]	-9.781 [-12.089 ; -7.528]

Body Fluids

A method comparison study was conducted to assess the performance of the Yumizen H2500 device when compared to the predicate device, Sysmex XN-Series (XN-10, XN-20) (K112605). A total of 427 residual body fluid specimens from pediatric (≤21 years) and adult subjects including a wide variety of disease states (clinical conditions) were tested across three (3) clinical sites (two (2) US sites and one (1) European site).

The study was conducted using 174 synovial fluids, 138 serous fluids and 115 cerebrospinal fluids from a wide range of demographics (age and sex) and disease states (clinical conditions). Study sites aimed to cover the target assay reportable range for the parameters.

Each specimen was analysed as soon as possible from the time of collection in two (2) replicates on the Yumizen H2500 and one (1) replicate on the Sysmex XN-10 System, when sufficient volume was available. Specimens were tested on the Yumizen H2500 and the Sysmex XN-Series (XN-10, XN-20) within two (2) hours of each other.

A Passing-Bablok regression analysis was performed. Bias at medical decision points were also evaluated for all sites combined. All results were within the predefined acceptance criteria and found to be acceptable. Overall, the Yumizen H2500 demonstrated comparable performance to the predicate device, Sysmex XN-Series (XN-10, XN-20) (K112605) in an intended use population in a clinical laboratory setting.

A summary of the results is presented in the tables below:

Table 23 – Synovial Body Fluid method comparison data summary

Parameter	N	Sample Range	r (95% CI)	Slope (95% CI)	Intercept (95% CI)
BFWBC (10^6/L)	159	22 - 8940	0.923 [0.9;0.946]	0.89 [0.86 ; 0.91]	26.37 [18.62 ; 39.67]
BFRBC (10^6/L)	75	1500 - 3520000	0.999 [0.999;0.999]	1.04 [1.0 ; 1.07]	-370.53 [-580.7 ; 61.48]
BFMN% (%)	143	9.0 - 98.0	0.967 [0.957;0.978]	0.90 [0.88 ; 0.91]	9.75 [8.13 ; 11.05]
BFMN# (10^6/L)	143	10 - 3140	0.943 [0.925;0.961]	1.09 [1.01 ; 1.25]	23.05 [9.94 ; 35.66]
BFPN% (%)	143	2.0 - 91.0	0.967 [0.957;0.978]	0.90 [0.88 ; 0.92]	0.64 [-0.29 ; 2.25]
BFPN# (10^6/L)	143	1 - 7430	0.911 [0.883;0.938]	0.79 [0.77 ; 0.82]	5.04 [1.68 ; 9.17]

Table 24 – Serous Body Fluid method comparison data summary

Parameter	N	Sample Range	r (95% CI)	Slope (95% CI)	Intercept (95% CI)
BFWBC (10^6/L)	135	14 - 9370	0.965 [0.954;0.977]	0.91 [0.89 ; 0.94]	14.89 [6.58 ; 23.34]
BFRBC (10^6/L)	87	1610 - 4590000	0.999 [0.999;1]	1.04 [1.02 ; 1.08]	31.75 [-231.53 ; 262.80]
BFMN% (%)	132	10.0 - 99.0	0.965 [0.954;0.977]	0.90 [0.85 ; 0.94]	11.66 [7.78 ; 15.94]
BFMN# (10^6/L)	132	23 - 4590	0.954 [0.939;0.969]	1.00 [0.96 ; 1.04]	13.31 [7.09 ; 21.67]
BFPN% (%)	132	1.0 - 90.0	0.965 [0.954;0.977]	0.90 [0.85 ; 0.95]	-1.58 [-2.69 ; -0.67]
BFPN# (10^6/L)	132	1 - 7560	0.972 [0.963;0.981]	0.78 [0.74 ; 0.82]	-1.36 [-2.82 ; 0.04]

Table 25 – CSF Body Fluid method comparison data summary

Parameter	N	Sample Range	r (95% CI)	Slope (95% CI)	Intercept (95% CI)
BFWBC (10^6/L)	109	5 - 8460	0.980 [0.973;0.988]	0.99 [0.95 ; 1.02]	5.14 [3.87 ; 7.25]
BFRBC (10^6/L)	71	1650 - 4690000	1.000 [1;1]	1.07 [1.04 ; 1.08]	15.80 [-533.69 ; 487.19]
BFMN% (%)	77	1 - 100	0.816 [0.738;0.887]	0.94 [0.88 ; 1.04]	10.87 [6.31 ; 14.89]
BFMN# (10^6/L)	77	6 - 2980	0.693 [0.566;0.8]	1.11 [1.00 ; 1.18]	6.36 [2.36 ; 11.25]
BFPN% (%)	77	0 - 99	0.817 [0.739;0.888]	0.94 [0.88 ; 1.05]	-5.36 [-13.33 ; -0.86]
BFPN# (10^6/L)	77	0 - 5940	0.863 [0.805;0.918]	0.87 [0.81 ; 0.99]	-0.49 [-2.46 ; 0.58]

b. Matrix Comparison:

Comparability between sampling types (capillary / venous)

The study was performed to demonstrate comparability between capillary whole blood samples and venous whole blood samples on the Yumizen H2500 device.
A total of 84 normal and pathological paired capillary and venous whole blood specimens were prospectively collected. Paired specimens collected from the same individuals were assayed in duplicate on the Yumizen H2500 device at one (1) clinical site. The clinical site aimed to enroll subject samples that covered all relevant medical decision points and were representative of the proposed analytical measurement ranges to the extent possible.
Bias was estimated at three points for each parameter: the low end of the distribution of observations, the mid-point, and the high end of the distribution, based on EP9-A3 guidelines. Acceptance criteria were met for all parameters at all levels. Therefore, the study results support the claim of using the two specimen types for measurement on the Yumizen H2500 device.

Comparability between body fluid anticoagulants

The study was performed to demonstrate comparability between body fluid anticoagulants on the Yumizen H2500 device.
A total of 9 synovial body fluids without anticoagulant, 39 synovial body fluids with K2EDTA anticoagulant, 92 synovial body fluids with Lithium Heparin anticoagulant and 34 synovial body fluids with Sodium Heparin anticoagulant were run on the Yumizen H2500 device at three (3) clinical sites. In the Bland-Altman difference plots, a visual examination of each anticoagulant subgroup of samples was performed. No difference linked to anticoagulant was observed on these graphs. No significant effect linked to the matrix was observed on these data.

A total of 82 serous body fluids without anticoagulant and 56 serous body fluids with K2EDTA were run on the Yumizen H2500 device at three (3) clinical sites.
In the Bland-Altman difference plots, a visual examination of each anticoagulant subgroup of samples was performed. No difference linked to anticoagulant was observed on these graphs. No significant effect linked to the matrix was observed on these data.

Comparability between analytical modes

The study was performed to demonstrate equivalency between Yumizen H2500 available analytical modes:

Table 26 - List of Yumizen H2500 Modes and cycles

Available Analytical Modes	Corresponding Analytical Cycle
DIF	DIF
DIR	DIR
RBC_PLTO	RBC_PLTO
DIF_LV	DIF_LV
CBC	DIF
RET	DIR
CBR	DIR

There are seven (7) analytical modes based on four (4) different cycles only. The equivalency between those four (4) cycles: DIF, DIR, RBC_PLTO and DIF_LV was verified.

A total of 166 normal and pathological residual whole blood specimens were assayed in duplicate in the DIR and DIF modes on one (1) Yumizen H2500 at one (1) clinical site to compare performance between analytical modes, and the results were analyzed for all applicable parameters.
A total of 172 normal and pathological residual whole blood specimens were assayed in duplicate in the RBC_PLTO and DIF modes one (1) Yumizen H2500 at one (1) clinical site to compare performance between analytical modes, and the results were analyzed for all applicable parameters.
A total of 187 normal and pathological residual whole blood specimens were assayed in duplicate in the DIF_LV and DIF modes on one (1) Yumizen H2500 at one (1) clinical site to compare performance between analytical modes, and the results were analyzed for all applicable parameters.
Study site aimed to cover the target assay reportable range for the parameters.
Bias was estimated at three points for each parameter: the low end of the distribution of observations, the mid-point, and the high end of the distribution, based on EP9-A3 guidelines. Acceptance criteria were met for all parameters at all levels.
The results show comparable performance characteristics for all Yumizen H2500 modes.

Comparability mode to mode

The study was performed to demonstrate comparability between automatic rack mode versus manual (STAT) mode with whole blood samples on the Yumizen H2500 device.
A total of 83 normal and pathological residual whole blood samples were run in automatic rack mode version manual (STAT) mode on the Yumizen H2500 device at one (1) clinical site. The clinical site aimed to enroll subject samples that covered all relevant medical decision points and were representative of the proposed analytical measurement ranges to the extent possible.
Bias was estimated at three points for each parameter: the low end of the distribution of observations, the mid-point, and the high end of the distribution, based on EP9-A3 guidelines. Acceptance criteria were met for all parameters at all levels.
The results show comparable performance characteristics for all Yumizen H2500 modes.

c. Clinical Sensitivity:

Flagging analysis was conducted to evaluate the flagging capabilities of the Yumizen H2500 using the flagging results obtained from the samples used in the method comparison study, from four (4) clinical sites, based on CLSI H20-A2 guidelines. A total of 456 residual normal (no flags, marked as negative) and abnormal (contained flags, marked as positive) whole blood samples were tested and compared to the reference (predicate or manual count results, depending on the parameter).

The results were classified according to the following categories:

TN (True negative): Yumizen H2500 result and reference result are both negative (normal sample).

TP (True positive): Yumizen H2500 result and reference result are both positive (abnormal sample).

FN (False Negative): Yumizen H2500 gives a negative result (normal sample) whereas reference gives a positive result (abnormal sample).

FP (False Positive): Yumizen H2500 gives a positive result (abnormal sample) whereas reference gives a negative result (normal sample).

The estimated sensitivity, estimated specificity and estimated efficiency were calculated for each pathology and abnormality, using the following calculations:

Estimated sensitivity (%): TP / (TP+FN) x 100
Estimated specificity (%): TN / (TN+FP) x 100
Estimated efficiency (%): (TP+TN) / (TP+FN+FP+TN) x 100

The overall flagging capabilities of the Yumizen H2500 device met the predefined acceptance criteria for both sensitivity and specificity.

A summary of the results is presented in the table below:

Table 27 - Clinical Sensitivity Study acceptance criteria

Category of Abnormalities	N	TP	FP	EN	TN	Sensitivity (95%CI)	Specificity (95%CI)	Efficiency (95%CI)
Any Morphological Flag	455	165	41	40	209	80.5% (74.5% to 85.3%)	83.6% (78.5% to 87.7%)	82.2% (78.4% to 85.6%)
Any Distributional Abnormality	456	306	9	27	114	91.9% (88.5% to 94.4%)	92.7% (86.7% to 96.1%)	92.1% (89.2% to 94.4%)
Any Morphological Flag and/or Distributional Abnormality	455	307	11	34	103	90.0% (86.4% to 92.8%)	90.4% (83.5% to 94.5%)	90.1% (87.0% to 92.7%)

C. Clinical Studies

Not applicable

D. Clinical Cut-Off

Not applicable.

E. Expected Values/Reference Range:

Whole Blood - Adult samples

The adult reference intervals study was conducted at two (2) US clinical sites to establish adult reference intervals for the Yumizen H2500 device. The study followed CLSI EP28-A3c guidelines and was performed using whole blood samples collected from 240 (120 male and 120 female) apparently healthy adults (>21 years). Each of the samples was analyzed on one Yumizen H2500 device for all parameters. The reference intervals were calculated for each parameter. The lower and upper limits of the 95% reference intervals were determined based on the 2.5th and 97.5th percentiles of all valid measurements for each sex group, respectively.

Table 28 - Whole blood – Adult reference intervals

Parameter	Female	Male
WBC (10^9/L) (10^3/µL)	4.71-12.03	4.00-10.74
RBC (10^{12}/L) (10^6/µL)	3.93-5.35	4.08-6.06
HGB (g/dL)	10.8-15.0	11.8-17.2
HCT (%)	33.8-46.2	35.9-50.6
MCV (fL)	77.8-95.8	69.5-96.5
MCH (pg)	25.2-32.0	22.3-32.2
MCHC (g/L)	313-344	313-347
RDW-SD (fL)	30.9-47.2	30.9-48.0
RDW-CV (%)	12.0-16.0	12.7-19.1
PLT (10^9/L) (10^3/µL)	183-402	144-379
MPV (fL)	8.0-11.2	7.3-11.6
TNC (10^9/L) (10^3/µL)	4.71-12.03	4.00-10.74
NRBC# (10^9/L) (10^3/µL)	0.00-0.00	0.00-0.00
NRBC% (%)	0.0-0.0	0.0-0.0
LYM# (10^9/L) (10^3/µL)	1.11-3.78	1.21-3.88
LYM% (%)	18.6-49.8	16.5-46.5
MON# (10^9/L) (10^3/µL)	0.27-0.97	0.28-1.04
MON% (%)	4.6-11.7	5.1-12.3
NEU# (10^9/L) (10^3/µL)	1.96-8.39	1.88-6.62
NEU% (%)	38.0-72.3	41.4-75.7
EOS# (10^9/L) (10^3/µL)	0.04-0.47	0.03-0.43
EOS% (%)	0.6-6.0	0.5-5.2
BAS# (10^9/L) (10^3/µL)	0.00-0.07	0.00-0.08
BAS% (%)	0.0-1.2	0.0-1.1
IMG# (10^9/L) (10^3/µL)	0.01-0.15	0.00-0.19
IMG% (%)	0.1-2.0	0.1-2.5
PLT-Ox (10^9/L) (10^3/µL)	175-420	134-370
LPF (%)	1.3-8.0	1.0-11.5
RET# (10^9/L) (10^3/µL)	26-118	27-137
RET% (%)	0.55-2.62	0.54-2.39
CRC (%)	0.50-2.35	0.53-2.49
IRF	0.00-0.16	0.01-0.20
RHCc (pg)	24.7-35.2	25.1-36.8

Whole Blood - Pediatric samples

The pediatric reference intervals study was conducted at two (2) US clinical sites to establish pediatric reference intervals for the Yumizen H2500 device. The study followed CLSI EP28-A3c guidelines and was performed using pediatric venous or capillary whole blood samples collected from at least 80 (approx. 40 male and 40 female) apparently healthy neonates, infants, children and adolescents (<22 years). Each of the samples was analyzed on one Yumizen H2500 device for all parameters. The Robust method is used to determine the most appropriate weighed mean and calculate the desired reference interval of all valid measurements for each age group, respectively.

Table 29 - Whole blood – Pediatric reference interval

Parameter	Neonate	Infant	Child	Adolescent
WBC (10^9/L) (10^3/µL)	4.28-18.62	5.11-13.99	1.87-12.54	3.40-10.40
RBC (10^{12}/L) (10^6/µL)	2.21-6.43	3.59-5.60	3.82-5.21	4.14-5.54
HGB (g/dL)	6.1-20.8	9.4-14.5	10.7-14.2	12.2-16.2
HCT (%)	19.9-65.0	29.2-44.9	31.7-44.0	37.6-48.6
MCV (fL)	78.8-119.9	70.9-91.4	75.3-93.6	80.5-97.9
MCH (pg)	24.9-38.7	22.5-30.2	24.5-31.1	26.4-32.4
MCHC (g/L)	306-334	312-335	307-353	312-343
RDW-SD (fL)	43.8-83.9	26.5-51.2	31.6-45.7	33.1-46.5
RDW-CV (%)	12.0-22.3	11.3-18.7	12.1-16.8	12.1-15.7
PLT (10^9/L) (10^3/µL)	55-564	123-610	175-452	147-398
MPV (fL)	7.7-12.4	6.6-11.5	7.6-10.6	7.4-11.5
TNC (10^9/L) (10^3/µL)	4.10-19.11	5.01-13.89	1.80-12.59	2.17-11.5
NRBC# (10^9/L) (10^3/µL)	0.00-0.00	0.00-0.00	0.00-0.00	2.17-11.39
NRBC% (%)	0.0-0.0	0.0-0.0	0.0-0.0	0.00-0.00
LYM# (10^9/L) (10^3/µL)	0.17-6.56	1.70-10.26	0-5.63	0.0-0.0
LYM% (%)	7.1-58.3	26.2-100.0	22.9-66.5	0.0-4.49
MON# (10^9/L) (10^3/µL)	0-3.29	0-1.91	0.21-0.96	0.14-0.93
MON% (%)	0-24.3	0-17.3	2.98-13.4	1.49-14.1
NEU# (10^9/L) (10^3/µL)	0-11.32	0-5.54	0-6.03	0.64-6.93
NEU% (%)	17.6-75.9	0-53.3	19.6-63.4	25.8-90.1
EOS# (10^9/L) (10^3/µL)	0-0.64	0-0.56	0-0.96	0-0.23
EOS% (%)	0-6.5	0-5.6	0-10.9	0-3.2
BAS# (10^9/L) (10^3/µL)	0-0.09	0-0.09	0-0.08	0-0.44
BAS% (%)	0-0.8	0-0.8	0-1.1	0-7.0
IMG# (10^9/L) (10^3/µL)	0-0.30	0-0.11	0-0.06	0-0.06
IMG% (%)	0.06-2.22	0-0.96	0.10-0.59	0-0.78
PLT-Ox (10^9/L) (10^3/µL)	0-610	96-593	177-433	142-382
LPF (%)	0-11.5	0-6.3	0-4.7	0-9.4
RET# (10^9/L) (10^3/µL)	0-388	16-91	18-76	12-90
RET% (%)	0-9.00	0.18-2.18	0.39-1.68	0.22-1.92
CRC (%)	0-9.08	0.24-1.69	0.33-1.41	0.24-1.77
IRF	0-0.42	0-0.16	0-0.14	0-0.55
RHCc (pg)	24.2-45.9	20.4-32.1	23.6-33.4	16.0-47.5

Body Fluids

The body fluid reference intervals study was conducted at two (2) clinical US sites to establish body fluid reference intervals for the Yumizen H2500 device. The study followed CLSI EP28-A3c guidelines and was performed using body fluid samples (Synovial, serous and cerebrospinal fluids) collected from at least 100 apparently healthy men and women. Each of the samples was analyzed on one Yumizen H2500 device for all parameters. The reference intervals were calculated for each parameter. The Robust method is used to determine the most appropriate weighed mean and calculate the desired reference interval of all valid measurements for each body fluid type, respectively.

Table 30 - Body fluid – Reference interval

Parameter	Synovial	Serous	CSF
BFWBC (10^6/L)	0-1902	0-951	0-301
BFRBC (10^6/L)	0-26275	0-13813	0-17679
BFPN# (10^6/L)	0-1358	0-384	0-188
BFPN% (%)	0-96	0-53	0-95
BFMN# (10^6/L)	0-864	0-672	0-217
BFMN% (%)	0-100	0-100	0-100

F. Other Supportive Instrument Performance Characteristics Data

Not applicable.

VIII. Proposed Labeling

The labeling is written as per the recommendations given in standard ISO 15223-1 and EN 18113-2. It takes into account the requirements of 21 CFR Part 809.10.

IX. Conclusion

As per 21CFR Part 807.92(b)(3), the nonclinical and clinical tests demonstrate that the Yumizen H2500 devices are as safe, as effective, and perform as well as the predicate device.

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