510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k141681

B. Purpose for Submission:

Clearance of Sysmex® XN-Series (XN-11, XN-21)

C. Manufacturer and Instrument Name:

Sysmex America, Inc.; Sysmex® XN-Series (XN-11, XN-21) Automated Hematology Analyzers

D. Type of Test or Tests Performed:

Quantitative test for white blood count (WBC), red blood count (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelets (PLT), neutrophil (NEUT)%/#, lymphocyte (LYMPH)%/#, monocyte (MONO)%/#, eosinophil (EO)%/#, basophil (BASO)%/#, immature granulocytes (IG)%/#, red cell distribution width coefficient variation (RDW-CV), red cell distribution width standard deviation (RDW-SD), mean platelet volume (MPV), nucleated red blood cells (NRBC)#/%, reticulocyte (RET)%/#, immature platelet fraction (IPF), immature reticulocyte information (IRF), reticulocyte hemoglobin (RET-He), white blood count body fluid (WBC-BF), red blood count body fluid (RBC-BF), mononuclear (MN)%/#, polymorphonuclear (PMN)%/#, and total cell count body fluid (TC-BF) parameters.

E. System Descriptions:

1. Device Description:
   The Sysmex® XN-Series modules (XN-11, XN-21) are multi-parameter hematology analyzers intended to perform tests on whole blood samples collected in K_2 or K_3EDTA anticoagulant and body fluids (pleural, peritoneal and synovial) collected in K_2 anticoagulant. Sysmex® XN-11 and XN-21 are part of the family of XN-Series devices (XN-10, XN-20 which were cleared under k112605) with technical modifications aimed to stabilize the HCT/MCV parameters to within +8% after storage at room temperature (18-26°C) for 24 hours and at refrigerated temperature (2-8°C) for 48 hours. These modifications include software and hardware updates as well as reagent modifications, i.e. CELLSHEATH(C). Software and hardware modifications include the addition of a heating block and changes to the instrument tubing. The listed modifications only impact the RBC/PLT and HGB dilution step: RBC/PLT and HGB will be diluted with CELLSHEATH(C) reagent after prewarming past 30°C.

The complete instrument consists of four principal units: (1) Two Main Units (XN-11, XN-21) which aspirate, dilute, mix, and analyze blood and body fluid samples; (2) Two Auto Sampler Units (SA-10 for a single module, or SA-20 for two modules) which supply samples to the Main Unit automatically; (3) IPU (Information Processing Unit) which processes data from the Main Unit and provides the operator interface with the system; (4) Pneumatic Unit which supplies pressure and vacuum from the Main Unit. Operator interface with the IPU is accomplished with the use of a 22-key panel keyboard.

Three configurations for the XN-Series modules are provided:

a. XN-1000 comprised of:
    1) XN-11
    2) XN-21
    3) SA-10 (Auto Sampler for single module)
b. XN-2000 comprised of:
    1) Two XN-11 or XN-21 or combination
    2) SA-20 (Auto Sampler for two modules)
c. XN-9000 comprised of:
    1) One to nine XN-11 or XN-21 or combination of both modules
    2) One to nine conveyors (CV), one for each XN module or Slide Preparation Unit (SP)
    3) SP-10 (Slide Preparation Unit)
    4) BT-40 (Barcode Terminal)

2. Principles of Operation:

The XN-Series analyzers perform analysis using the following methods: Sheath Flow DC Detection Method, and Flow Cytometry Methods using a Semiconductor Laser and Sodium Lauryl Sulfate (SLS)-hemoglobin. Cells pass through the aperture of the detector surrounded by sheath fluid using the sheath flow method. The principle of flow cytometry is also used. A semiconductor laser beam is emitted to the cells passing through the flow cell. The forward scattered light is received by the photodiode; the lateral scattered light and lateral fluorescent light are received by the photo multiplier tube. This light is converted into electrical pulses, thus making it possible to obtain cell information. Particle characterization and identification is based on detection of forward scatter, fluorescence and adaptive cluster analysis. The system carries out all processes automatically from aspiration of the sample to outputting results and uses Microsoft Windows Operating System.

The body fluid analysis mode of the XN-Series analyzers uses the 4 part differential scattergram and the RBC distribution obtained from a specialized analysis sequence to calculate and display the WBC (WBC-BF) counts, mononuclear cell (MN) / polymorphonuclear cell (PMN) counts and percentages, TC-BF (Total Count) & RBC (RBC-BF) counts found in the body fluid.

Analysis results and graphics are displayed on the IPU screen. They can be printed on any of the available printers or transmitted to a host computer.

3. Modes of Operation:
   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?
   Yes ___x_____ or No _____
   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?
   Yes _____ or No ____x____

4. Specimen Identification:
   Specimen identification input is manual (by operator) or by barcode reader.

5. Specimen Sampling and Handling:
   There are two modes of sample introduction: (1) Sampler Mode; (2) Manual Mode. Each analysis mode uses the same single fluidic and aspiration pathway.

   In the Sampler Analysis Mode the operator loads the sample tubes into a rack, which is then automatically transported and analyzed by the instrument. This mode automatically mixes, aspirates, and analyzes samples without removing their caps.
   In the Manual Analysis Mode, there are two sample tube holders: (1) Normal sample tube holder; (2) Micro collection tube holder. In this mode the operator loads and mixes the samples tubes individually by hand.
   - In the Normal Sample Tube Holder position, whole blood and body fluid samples can be analyzed with cap on or cap off.
   - The Micro Collection Tube Holder position is used for analyzing a minute amount of whole blood or whole blood after diluting the sample to 1:7 that has been collected in a micro collection tube. Samples are analyzed with cap off in this position.
   - Low WBC Count (LWBC) Mode is used for retesting whole blood samples with low white blood cell counts based on user defined rules criteria. The counting time is set to 3 times that of the Whole Blood mode to increase white blood cell measurement accuracy at very low counts.

6. Calibration:
   The XN CAL™ calibrator (k141962) is used for calibration of the instrument for WBC, RBC, HGB, HCT, PLT and RET. XN CAL PF™ (k141955) is used for calibration of the instrument for PLT-F (platelet count obtained from the PLT-F channel). Calibration is performed as needed (e.g., when QC data is fluctuating) to ensure accuracy of the system.

7. Quality Control:
   The XN CHECK™ (k141964) whole blood quality control material (three levels) and the XN BF CHECK™ (k141957) body fluid quality control material (two levels) are used to monitor the performance of the XN-Series analyzers. Quality control should be run according to licensing agency regulations.

8. Software:
   FDA has reviewed applicant's Hazard Analysis and Software Development processes for

this line of product types:
Yes___X___ or No_____

F. Regulatory Information:

1. Regulation section:
   21 CFR 864.5220, Automated differential cell counter

2. Classification:
   Class II

3 Product code:
   GKZ, Counter, differential cell

4. Panel:
   Hematology (81)

G. Intended Use:

7. Indication(s) for Use:
   The XN-Series modules (XN-11, XN-21) are quantitative multi-parameter automated hematology analyzers intended for in vitro diagnostic use in screening patient populations found in clinical and reference laboratories.

   The XN-Series modules classify and enumerate the following parameters in whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, 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 body fluids (peritoneal, pleural and synovial). Whole blood should be collected in K_2 or K_3EDTA anticoagulant and peritoneal, pleural and synovial fluids in K_2EDTA anticoagulant to prevent clotting of fluid.

2. Special Conditions for Use Statement(s):
   For prescription use only.

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:
   Sysmex® XE-5000 Automated Hematology Analyzer; k071967

2. Comparison with Predicate Device:

Similarities		
Item	Device XN-Series (XN-11, XN-21)	Predicate XE-5000 (k071967)
Intended Use	The Sysmex® XN-Series modules (XN-11, XN-21) are quantitative multi-parameter automated hematology analyzers intended for in vitro diagnostic use in screening patient populations found in clinical and reference laboratories. The XN-Series modules classify and enumerate the following parameters in whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, 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 body fluids (peritoneal, pleural and synovial fluids). Whole blood should be collected in K_2 or K_3EDTA anticoagulant and, peritoneal, pleural and synovial fluids in K_2EDTA anticoagulant to prevent clotting of fluid.	Sysmex® XE-5000 is an automated hematology analyzer for in vitro diagnostic use in screening patient populations found in clinical laboratories. The XE-5000 classifies and enumerates the same parameters as the XE-2100 (K992875) using whole blood as described below, cord blood for HPC and has a body fluid mode for body fluids. The Body Fluid mode analyzes WBC-BF, RBC-BF, MN%/#, PMN%/# and TC-BF in body fluids (cerebrospinal fluids (CSF), serous fluids, and synovial fluids with EDTA, as needed). WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT% / #, LYMPH% / #, MONO% / #, EO% / #, BASO% / #, NRBC% / #, RDW-SD, RDW-CV, MPV, RET% / #, IRF, IG% / #, RET-He, IPF, HPC WBC-BF, RBC-BF, MN% / #, PMN%/ #, TC-BF#.
Specimen Type	Whole Blood and Body Fluids	Same
Test Principle	Performs hematology analyses according to the Hydro Dynamic Focusing (DC Detection), flow cytometry method (using a semiconductor laser), and SLS-hemoglobin method.	Same
Parameters	Whole Blood Mode: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, NRBC%/#, RDW-CV, RDW-SD, MPV, RET%/#, IRF, IG%/#, RET-He, IPF. Body Fluid Mode: WBC-BF, RBC-BF, MN%/#, PMN%/#, TC-BF	Same
Reagents	SULFOLYSER (Lyse)	Same

Similarities		
Item	Device XN-Series (XN-11, XN-21)	Predicate XE-5000 (k071967)
Mode of Operation	Sampler Analysis Mode Manual Closed Analysis Mode Body Fluid Analysis Mode	Same
Measuring Channels	RBC/RET/PLT	Same

Differences		
Item	Device XN-Series (XN-11, XN-21)	Predicate XE-5000 (k071967)
Specimen type	Not Available Not Available	Body Fluid – CSF Umbilical Cord Blood
Test Principal	Not Available	RF/DC detection method
Controls & Calibrators	**Whole Blood** XN CHECK – 3 Levels XN CAL (XN-Series Calibrator) XN CAL PF (Platelet F Calibrator) **Body Fluid** XN CHECK BF – 2 Levels	**Whole Blood** e-Check (XE) – 3 Levels X CAL (XE Calibrator) Not Available **Body Fluid** Not Available
IPU	Multi-Module connect	Single Module connect
Modes of Operation	Manual Open Cap Analysis Mode (Sample placed in tube holder position) Pre-dilute Analysis Mode Dilute sample 1:7 Low WBC Mode (LWBC)	Manual Open Cap Analysis Mode (Operator presents sample to aspiration needle) Capillary Analysis Mode Dilute sample 1:5 Not Available
Parameters	Not Available	HPC
Sample Aspiration/ Fluidic Pathway	Single pathway	Two pathways
Software/Hardware	Rules-based rerun/reflex	Not Available
Throughput	**Whole Blood** 100 samples/hour maximum depending on mode used. **Body Fluid** 40 samples/hour maximum	**Whole Blood** Approximately 113-150 depending on mode used. **Body Fluid** 38 samples/hour
Measuring Channels	WNR,WDF, WNR, WPC (Not available on XN-11) PLT-F	WBC/BASO, DIFF, NRBC, IMI Not Available
Reagents	CELLPACK® DCL (Diluent) CELLPACK™ DFL (Diluent) CELLSHEATH(C)™ (Diluent) Lysercell™ WNR (Lyse) Lysercell™ WDF (Lyse) Lysercell™ WPC* (Lyse)	CELLPACK® (Diluent) CELLSHEATH™ (Diluent) Not Available STROMATOLYSER™-FB (Lyse) STROMATOLYSER™-4DL (Lyse) STROMATOLYSER™-

Differences		
Item	Device XN-Series (XN-11, XN-21)	Predicate XE-5000 (k071967)
	Fluorocell™ WNR (Stain) Fluorocell™ WDF (Stain) Fluorocell™ RET (Stain) Fluorocell™ PLT (Stain) Fluorocell™ WPC* (Stain) *Not used on XN-11 module	4DS (Stain) STROMATOLYSER™-NR (Diluent) STROMATOLYSER™-NR (Stain) RET-SEARCH II (Diluent) RET-SEARCH II (Stain) STROMATOLYSER™- IM (Lyse)
Sample Aspiration Volume	Sampler Mode - 88µL Manual (Closed Cap) Mode - 88µL Manual (Open Cap) Mode - 88µL Dilution Mode - 70µL Body Fluid Mode - 88µL	Sampler Mode - 200µL Manual (Closed Cap) Mode - 200µL Manual (Open Cap) Mode - 130µL Capillary Mode - 130µL Body Fluid Mode - 130µL

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

CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition

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

CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

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

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

CLSI H56-A, Body Fluid Analysis for Cellular Composition; Approved Guideline

CLSI EP12-A2, User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline-Second Edition

CLSI C24-A3, Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline-Third Edition

CLSI EP9-A2, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition

CLSI EP9-A3, Measurement Procedure Comparison and BIAS Estimation Using Patient Samples; Approved Guideline-Third Edition

CLSI EP17-A, Protocol for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline 2004

CLSI H18-A3, Procedures for the Handling and Processing of Blood Specimens; Approved Guideline-Third Edition

CLSI C28-A3, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition

J. Performance Characteristics*:*

1. Analytical Performance:

a. Method comparison:

Whole Blood

Method comparison studies were performed to access the performance of the XN-Series (XN-11, XN-21) analyzers when compared to the XE-5000 (predicate device). The XN-11 and XN-21 analyzers are the same as the XN-Series (XN-10, XN-20) analyzers (k112605) with modifications to stabilize the HCT/MCV parameter to within +8% at room temperature (18°-26°C) for 24 hours and at refrigerated temperature (2-8°C) for 48 hours for commercial and reference laboratories. The changes only impact the RBC/PLT and HGB dilution step. The WBC (WNR, WDF, WPC), RET and PLT-F measuring channels do not use the CELLSHEATH(C) reagent and therefore are not impacted. Method Comparison studies were performed to evaluate the performance of the RBC, HGB, HCT/MCV and PLT-I parameters on the XN-11 and XN-21 Series analyzers when compared to the XE-5000. The method comparison studies consisted of a total of 299 residual K_2EDTA whole blood samples collected by three (3) U.S. sites. All samples were run in the Automated Sampling Mode in singlet on the XE-5000 and within two hours on the XN-11 and XN-21 Series analyzers. Samples covered clinical medical decision levels and of the full reportable measuring ranges of the XN-11 and XN-21 Series analyzers. The results of the linear regression and bias analyses between the XE-5000 and the XN-11, XN-21 Series Whole Blood Mode met the acceptance criteria for all applicable parameters. An example of the results between XN-11 and XE-5000 is shown below and comparable results were obtained with the XN-21.

Correlation and Estimated Bias (Whole Blood – combined sites): (XE-5000 vs. XN-11)

Measurand	N	Result Range	r	Slope (95% CI)	Intercept (95% CI)	Mean Diff	Mean %Diff
WBC ($10^3/\mu L$)	299	0.68-387.67	0.9998	1.033 (1.031, 1.035)	-0.316 (-0.378, -0.254)	0.06	0.5
MPV (fL)	299	8.4-14.2	0.8426	1.235 (1.155, 1.315)	-2.63 (-3.49, -1.77)	-0.11	-1.0
RET (%)	299	0.10-10.88	0.9462	0.984 (0.946,1.021)	-0.062 (-0.151,0.028)	-0.90	-4.6
IRF (%)	299	0.0-51.4	0.8958	0.847 (0.802,0.892)	1.17 (0.31,2.02)	-1.26	-7.8
PLT-F ($10^3/\mu L$)	299	11-1416	0.9931	1.011 (0.997,1.025)	0.2 (-3.7,4.0)	2.8	1.1
NEUT (%)	299	0.0-98.2	0.9851	0.973 (0.954,0.992)	3.13 (1.84,4.41)	1.39	2.1
LYMPH (%)	299	1.0-93.6	0.9841	0.990 (0.970,1.010)	-0.72 (-1.28,-0.16)	-0.96	-4.0
MONO (%)	299	0.2-71.0	0.9557	0.967 (0.934,1.000)	-0.25 (-0.63,0.13)	-0.56	-5.9
EO (%)	299	0.0-26.0	0.9873	0.987 (0.969,1.005)	0.03 (-0.03,0.10)	0.01	0.4
BASO (%)	299	0.0-10.8	0.8369	0.745 (0.695,0.795)	0.23 (0.19,0.28)	0.11	22.4
NRBC (%)	299	0.0-12.3	0.9463	0.845 (0.813,0.877)	0.064 (0.031,0.096)	0.03	13.0
IG (%)	299	0.0-18.1	0.9161	1.228 (1.171,1.285)	0.13 (-0.03,0.29)	0.42	32.8
RDW-CV (%)	299	11.4-26.9	0.9577	0.831 (0.804,0.859)	1.42 (0.98,1.86)	-1.25	-8.0
RDW-SD (fL)	299	35.5-96.0	0.9332	0.760 (0.728,0.792)	8.22 (6.56,9.87)	-3.9	-7.7
RET-He (pg)	299	18.3-43.4	0.9443	0.906 (0.871,0.941)	1.60 (0.45,2.75)	-1.45	-4.4
IPF (%)	299	0.9-32.0	0.8865	0.856 (0.808,0.904)	-0.33 (-0.63,-0.03)	-1.3	-27.4
RBC ($10^6/\mu L$)	Site 1 106	1.21-6.15	0.9979	1.069 (1.056,1.083)	-0.186 (-0.239,-0.133)	0.08	2.0
	Site 2 93	1.28-6.43	0.9950	1.047 (1.026,1.069)	-0.223 (-0.310,-0.137)	-0.04	-1.0
	Site 3 100	2.27-5.85	0.9986	1.033 (1.022,1.043)	-0.168 (-0.209,-0.127)	-0.04	-1.3
HGB (g/dL)	Site 1 106	3.8-18.2	0.9991	1.014 (1.006,1.022)	-0.12 (-0.22,-0.03)	0.04	0.3
	Site 2 93	4.1-19.6	0.9992	1.004 (0.996,1.013)	0.09 (-0.01,0.18)	0.14	1.2
	Site 3 100	7.3-17.3	0.9991	0.997 (0.989,1.005)	-0.05 (-0.14,0.04)	-0.08	-0.7
HCT (%)	Site 1 106	11.4-51.5	0.9951	1.041 (1.021,1.061)	-1.30 (-2.01,-0.60)	0.10	0.2
	Site 2 93	12.0-58.9	0.9924	1.059 (1.032,1.086)	-2.48 (-3.44,-1.51)	-0.48	-1.3
	Site 3 100	22.6-50.1	0.9884	1.066 (1.034,1.099)	-2.34 (-3.46,-1.22)	-0.10	-0.2
MCV (fL)	Site 1 106	65.0-112.9	0.9664	0.896 (0.850,0.941)	7.73 (3.70,11.75)	-1.54	-1.7
	Site 2 93	67.3-106.6	0.9296	0.978 (0.902,1.055)	1.74 (-5.19,8.67)	-0.32	-0.3
	Site 3 100	72.4-116.3	0.9566	0.870 (0.818,0.921)	12.80 (8.05,17.56)	0.81	0.8

Measurand	N	Result Range	r	Slope (95% CI)	Intercept (95% CI)	Mean Diff	Mean %Diff
PLT-I ($10^3/\mu L$)	Site 1 106	44-594	0.9919	0.968 (0.944,0.992)	1.3 (-5.4,7.9)	-7.1	-2.8
	Site 2 93	2-1243	0.9894	0.987 (0.957,1.016)	-4.987 (-14.194,4.221)	-10.0	-4.1
	Site 3 100	9-753	0.9952	0.954 (0.935,0.972)	2.4 (-3.0,7.7)	-8.9	-3.8
MCH (pg)	Site 1 106	20.1-39.0	0.9744	1.038 (0.992,1.084)	-1.56 (-2.94,-0.18)	-0.42	-1.3
	Site 2 93	21.7-33.3	0.9108	1.070 (0.976,1.163)	-1.21 (-3.96,1.54)	0.82	2.8
	Site 3 100	20.9-37.9	0.9886	1.026 (0.995,1.057)	-0.57 (-1.49,0.36)	0.21	0.7
MCHC (g/dL)	Site 1 106	30.4-37.4	0.8015	0.832 (0.728,0.936)	5.77 (2.23,9.31)	0.07	0.2
	Site 2 93	28.2-35.3	0.5041	1.330 (1.070,1.589)	-9.68 (-18.09,-1.27)	1.01	3.1
	Site 3 100	26.6-35.3	0.8102	0.742 (0.648,0.837)	8.19 (5.14,11.25)	-0.11	-0.3

Body Fluid

Method Comparison studies were performed to evaluate the performance of the Body Fluid Mode RBC-BF parameter of the XN-Series (XN-11, XN21) when compared to the XE-5000 using a total of 299 residual body fluid samples at three U.S sites. The body fluids (peritoneal, pleural, and synovial) were collected in K_2EDTA anticoagulant. All samples were run in singlet on the XE-5000 and within two hours on the XN-11 and XN-21 analyzers. The samples used in this study covered the full reportable measuring ranges to the extent possible of the XN-11 and XN-21 analyzers. The estimation of the bias of the body fluids collected met the bias limits. Shown below are comparison results for XN-11. Similar results were obtained for XN-21.

Correlation and Estimated Bias (Body Fluid – combined sites): (XE-5000 vs. XN-11)

Fluid Type	Measurand	N	Result Range	r	Slope (95% CI)	Intercept (95% CI)	Mean Diff	Mean %Diff
Pleural	WBC-BF ($10^3/\mu L$)	106	0.002-12.232	0.9858	1.035 (1.001,1.069)	-0.0295 (-0.1229,0.0639)	0.020	1.4
	TC-BF ($10^3/\mu L$)	106	0.002-12.233	0.9856	1.038 (1.004,1.073)	-0.0259 (-0.1223,0.0705)	0.031	2.0
	RBC-BF ($10^6/\mu L$)	106	0.000-3.300	0.9995	1.002 (0.996,1.008)	-0.0022 (-0.0054,0.0010)	-0.001	-0.9
	MN# ($10^3/\mu L$)	106	0.000-4.077	0.9601	0.997 (0.942,1.052)	0.0177 (-0.0400,0.0754)	0.016	1SD
	MN (%)	106	0.0-100.0	0.9166	1.085 (0.999,1.171)	-1.34 (-6.61,3.94)	3.4	1SD
	PMN# ($10^3/\mu L$)	106	0.000-10.703	0.9836	1.057 (1.020,1.094)	-0.0415 (-0.1203,0.0373)	0.004	1SD
	PMN (%)	106	0.0-100.0	0.9162	1.085 (0.999,1.171)	-7.20 (-11.65,-2.74)	-3.4	1SD
Peritoneal	WBC-BF ($10^3/\mu L$)	75	0.002-12.412	0.9978	1.004 (0.989,1.020)	-0.0133 (-0.0627,0.0362)	-0.007	-0.5
	TC-BF ($10^3/\mu L$)	75	0.002-12.425	0.9975	1.004 (0.987,1.020)	-0.0113 (-0.0635,0.0408)	-0.006	-0.4
	RBC-BF ($10^6/\mu L$)	75	0.000-3.430	0.9999	1.018 (1.015,1.021)	-0.0006 (-0.0025,0.0013)	0.003	1.5

Fluid Type	Measurand	N	Result Range	r	Slope (95% CI)	Intercept (95% CI)	Mean Diff	Mean %Diff
	MN# ($10^3/\mu L$)	75	0.001-2.741	0.9247	1.267 (1.153,1.381)	-0.0417 (-0.0997,0.0162)	0.023	1SD
	MN (%)	75	4.0-92.4	0.8781	1.191 (1.055,1.327)	-3.47 (-11.00,4.06)	6.0	1SD
	PMN# ($10^3/\mu L$)	75	0.001-10.760	0.9932	0.974 (0.948,1.001)	-0.0058 (-0.0774,0.0658)	-0.033	1SD
	PMN (%)	75	7.6-96.0	0.8787	1.192 (1.056,1.326)	-15.74 (-23.30,-8.17)	-6.1	1SD
Synovial	WBC-BF ($10^3/\mu L$)	89	0.004-23.403	0.9906	0.919 (0.892,0.946)	-0.0072 (-0.1599,0.1456)	-0.256	-8.33
	TC-BF ($10^3/\mu L$)	89	0.004-23.410	0.9906	0.918 (0.891,0.945)	0.0128 (-0.1410,0.1666)	-0.242	-7.77
	RBC-BF ($10^6/\mu L$)	89	0.000-5.962	0.9998	1.023 (1.019,1.027)	-0.0046 (-0.0086,-0.0006)	0.002	0.8
	MN# ($10^3/\mu L$)	89	0.001-7.664	0.9594	0.874 (0.820,0.927)	-0.0096 (-0.0934,0.0742)	-0.118	1SD
	MN (%)	89	4.2-96.1	0.9333	1.108 (1.022,1.194)	-1.59 (-5.89,2.71)	3.0	1SD
	PMN# ($10^3/\mu L$)	89	0.001-20.145	0.9894	0.952 (0.923,0.982)	-0.0276 (-0.1610,0.1058)	-0.132	1SD
	PMN (%)	89	3.9-95.8	0.9333	1.108 (1.022,1.194)	-9.21 (-14.62,-3.81)	-3.0	1SD

Flagging capabilities

Clinical sensitivity/specificity studies were conducted to evaluate the flagging capabilities of the XN-11, XN-21 analyzers using patient samples representing a variety of abnormal conditions in comparison to the XE-5000. The results of the XN-11, XN-21 analyzers flagging to the XE-5000 flagging evaluation were divided into two categories: (1) Normal, healthy adults – No Flags, Negative Judgment (2) Patients with positive morphology/Differential – Flags present, Positive Judgment. The results obtained from the flagging comparison study met the specification of ≥90.0% Agreement. Note: XN-11, XN-21 Site 2, eight (8) samples were removed due to protocol deviation and three (3) for incomplete results. XN-11, XN-21 Site 3, 14 samples were removed due to protocol deviation and one (1) for incomplete results. Total number of samples excluded or missing = 26.

Overall Flagging Analysis – XE-5000 vs. XN-11 – Combined sites

All Sites (N=299)		XE-5000		
		Positive (Abnormal)	Negative (Normal)	Total
XN-11	Positive (Abnormal)	156	5	161
	Negative (Normal)	4	134	138
	Total	160	139	299

Positive Percent Agreement (PPA) = 156/(156 + 4) x 100 = 97.5%
Negative Percent Agreement (NPA) = 134/(134 + 5) x 100 = 96.4%
Overall Agreement = (156+134/299) x100= 97.0%

Overall Flagging Analysis – XE-5000 vs. XN-21 – Combined sites

All Sites (N=299)		XE-5000		
		Positive (Abnormal)	Negative (Normal)	Total
XN-21	Positive (Abnormal)	157	7	164
	Negative (Normal)	3	132	135
	Total	160	139	299

Positive Percent Agreement (PPA) = 157/(157 + 3) x 100= 98.1%
Negative Percent Agreement (NPA) = 132/(132 + 7) x 100= 95.0%
Overall Agreement = (157+132/299) x100= 96.7%

b. Precision/Reproducibility:

Precision/Repeatability Study – Whole Blood Mode
Within-run precision studies of the direct measurement parameters RBC, HGB, HCT, and PLT-I which use CELLSHEATH(C) diluent were evaluated by using residual K_2EDTA whole blood samples around medical decision levels and the upper and lower limit of the analytical measuring range. Ten replicates of each sample were tested in the whole blood manual mode at three clinical sites. The mean, standard deviation (SD), and coefficient of variation (CV) were calculated for each sample. All sites met manufacturer's specifications (CV%) for precision.

Precision/Reproducibility – Whole Blood Mode
Evaluation of whole blood reproducibility for RBC, HGB, HCT/MCV and PLT-I parameters which use the CELLSHEATH(C) reagent was assessed using three levels of quality control material (Low, Normal, and High) performed on the XN-11 and XN-21 analyzers. Each level was run in duplicate twice each day for the length of the study or a minimum of 20 days using a single lot of control, calibration and reagent at each of the three test sites. Controls were automatically mixed by the analyzers before sampling. Results of the whole blood reproducibility included the precision results for each site separately and then combined data to show the within-run, between-run, between-day, between-site and total imprecision. Both XN-11 and XN-21 have similar results and met the acceptance criteria. Table below summarizes results from XN-11.

Whole Blood Reproducibility – Combined Sites- XN- 11 Module

All Sites Combined				Within-Run		Between-Run		Between-Day		Between-Site		Total	
Measurand	Control Level	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC ($x\ 10^3/\mu L$)	Level 1	272	2.790	0.055	1.97	0.000	0.00	0.024	0.87	0.064	2.29	0.088	3.14
	Level 2	259	7.179	0.087	1.21	0.034	0.47	0.032	0.44	0.154	2.14	0.183	2.54
	Level 3	271	17.22	0.187	1.08	0.000	0.00	0.133	0.77	0.546	3.17	0.593	3.44
RBC ($x\ 10^6/\mu L$)	Level 1	272	2.203	0.016	0.73	0.010	0.46	0.007	0.33	0.002	0.11	0.021	0.94
	Level 2	259	4.260	0.028	0.65	0.011	0.27	0.013	0.31	0.008	0.19	0.034	0.80
	Level 3	271	5.228	0.034	0.65	0.000	0.00	0.020	0.38	0.023	0.45	0.046	0.87
HGB (g/dL)	Level 1	272	5.896	0.053	0.89	0.000	0.00	0.020	0.34	0.045	0.77	0.072	1.22
	Level 2	259	12.02	0.059	0.49	0.031	0.26	0.050	0.42	0.124	1.03	0.149	1.24
	Level 3	271	16.34	0.073	0.45	0.036	0.22	0.054	0.33	0.197	1.21	0.220	1.35
HCT (%)	Level 1	272	17.69	0.156	0.88	0.111	0.63	0.138	0.78	0.197	1.12	0.308	1.74
	Level 2	259	34.53	0.261	0.75	0.219	0.64	0.224	0.65	0.471	1.36	0.623	1.80
	Level 3	271	46.55	0.392	0.84	0.201	0.43	0.374	0.80	0.709	1.52	0.914	1.96
MCV (fL)	Level 1	272	80.30	0.324	0.40	0.233	0.29	0.516	0.64	0.773	0.96	1.011	1.26
	Level 2	260	81.06	0.272	0.34	0.357	0.44	0.445	0.55	0.951	1.17	1.141	1.41
	Level 3	272	89.05	0.331	0.37	0.358	0.40	0.498	0.56	0.969	1.09	1.194	1.34
MCH (pg)	Level 1	272	26.76	0.272	1.02	0.000	0.00	0.089	0.33	0.230	0.86	0.368	1.37
	Level 2	260	28.22	0.227	0.80	0.136	0.48	0.073	0.26	0.335	1.19	0.433	1.53
	Level 3	272	31.27	0.256	0.82	0.000	0.00	0.145	0.46	0.500	1.60	0.580	1.86
MCHC (g/dL)	Level 1	272	33.32	0.383	1.15	0.113	0.34	0.255	0.76	0.512	1.54	0.697	2.09
	Level 2	260	34.84	0.294	0.84	0.238	0.68	0.185	0.53	0.831	2.38	0.931	2.67
	Level 3	272	35.12	0.328	0.93	0.082	0.23	0.315	0.90	0.953	2.71	1.059	3.02
PLT-I ($x\ 10^3/\mu L$)	Level 1	271	54.52	2.577	4.73	0.000	0.00	1.711	3.14	0.999	1.83	3.251	5.96
	Level 2	259	206.2	4.630	2.25	1.811	0.88	4.468	2.17	5.550	2.69	8.688	4.21
	Level 3	271	492.9	7.574	1.54	0.000	0.00	4.926	1.00	17.01	3.45	19.257	3.91
PLT-F ($x\ 10^3/\mu L$)	Level 1	272	54.50	2.540	4.66	0.000	0.00	1.692	3.11	1.015	1.86	3.217	5.90
	Level 2	259	206.2	4.630	2.25	1.811	0.88	4.468	2.17	5.550	2.69	8.688	4.21
	Level 3	271	492.9	7.574	1.54	0.000	0.00	4.926	1.00	17.01	3.45	19.257	3.91
RDW-SD (fL)	Level 1	272	46.27	0.400	0.87	0.167	0.36	0.362	0.78	0.445	0.96	0.719	1.55
	Level 2	260	42.66	0.344	0.81	0.222	0.52	0.320	0.75	0.409	0.96	0.662	1.55
	Level 3	272	44.96	0.276	0.61	0.000	0.00	0.219	0.49	0.436	0.97	0.561	1.25
RDW-CV (%)	Level 1	272	16.08	0.096	0.60	0.030	0.18	0.000	0.00	0.057	0.36	0.116	0.72
	Level 2	260	14.81	0.082	0.56	0.000	0.00	0.020	0.13	0.048	0.32	0.097	0.66
	Level 3	272	13.97	0.065	0.47	0.000	0.00	0.040	0.29	0.046	0.33	0.089	0.64
MPV (fL)	Level 1	272	8.951	0.276	3.09	0.026	0.29	0.224	2.50	0.639	7.14	0.732	8.17

All Sites Combined				Within-Run		Between-Run		Between-Day		Between-Site		Total	
Measurand	Control Level	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
	Level 2	260	10.89	0.135	1.24	0.040	0.36	0.332	3.05	0.648	5.95	0.741	6.81
	Level 3	272	10.53	0.076	0.72	0.000	0.00	0.208	1.97	0.815	7.73	0.844	8.01
NEUT#	Level 1	272	1.107	0.036	3.28	0.009	0.86	0.016	1.45	0.024	2.16	0.047	4.27
	Level 2	259	3.123	0.069	2.22	0.000	0.00	0.021	0.66	0.069	2.20	0.100	3.20
	Level 3	271	8.438	0.189	2.24	0.000	0.00	0.096	1.14	0.254	3.01	0.331	3.92
NEUT%	Level 1	272	39.69	1.058	2.67	0.000	0.00	0.411	1.04	0.049	0.12	1.136	2.86
	Level 2	260	43.51	0.851	1.96	0.000	0.00	0.270	0.62	0.126	0.29	0.902	2.07
	Level 3	272	49.01	0.926	1.89	0.000	0.00	0.358	0.73	0.310	0.63	1.040	2.12
LYMPH#	Level 1	272	0.929	0.052	5.64	0.000	0.00	0.014	1.50	0.018	1.91	0.057	6.14
	Level 2	259	1.985	0.077	3.86	0.000	0.00	0.022	1.13	0.011	0.57	0.081	4.06
	Level 3	271	3.852	0.117	3.05	0.043	1.11	0.018	0.47	0.094	2.45	0.158	4.09
LYMPH%	Level 1	272	33.20	1.501	4.52	0.000	0.00	0.213	0.64	0.199	0.60	1.530	4.61
	Level 2	260	27.66	1.011	3.66	0.000	0.00	0.126	0.45	0.406	1.47	1.097	3.97
	Level 3	272	22.36	0.703	3.14	0.154	0.69	0.000	0.00	0.153	0.69	0.735	3.29
MONO#	Level 1	272	0.352	0.039	10.97	0.000	0.00	0.006	1.75	0.017	4.96	0.043	12.17
	Level 2	259	0.970	0.068	7.06	0.021	2.12	0.000	0.00	0.057	5.85	0.091	9.41
	Level 3	271	2.098	0.111	5.28	0.040	1.88	0.000	0.00	0.119	5.67	0.167	7.97
MONO%	Level 1	272	12.62	1.370	10.86	0.000	0.00	0.211	1.67	0.393	3.11	1.441	11.42
	Level 2	260	13.50	0.930	6.89	0.239	1.77	0.000	0.00	0.504	3.74	1.085	8.04
	Level 3	272	12.18	0.615	5.05	0.245	2.01	0.000	0.00	0.325	2.67	0.738	6.06
EO#	Level 1	272	0.271	0.020	7.34	0.000	0.00	0.006	2.07	0.005	2.02	0.021	7.89
	Level 2	259	0.755	0.056	7.42	0.000	0.00	0.014	1.87	0.011	1.48	0.059	7.79
	Level 3	271	1.997	0.145	7.26	0.045	2.26	0.029	1.43	0.064	3.18	0.167	8.37
EO%	Level 1	272	9.726	0.687	7.07	0.053	0.55	0.219	2.25	0.000	0.00	0.723	7.44
	Level 2	260	10.52	0.762	7.24	0.000	0.00	0.194	1.84	0.133	1.26	0.797	7.58
	Level 3	272	11.61	0.834	7.19	0.286	2.46	0.143	1.23	0.126	1.09	0.902	7.77
BASO#	Level 1	272	0.133	0.005	4.10	0.001	1.02	0.001	0.47	0.003	2.26	0.006	4.82
	Level 2	259	0.346	0.009	2.71	0.002	0.63	0.003	0.85	0.008	2.20	0.013	3.65
	Level 3	271	0.834	0.019	2.30	0.000	0.00	0.005	0.61	0.027	3.29	0.034	4.06
BASO%	Level 1	272	4.767	0.181	3.79	0.029	0.61	0.000	0.00	0.012	0.25	0.183	3.84
	Level 2	260	4.817	0.125	2.59	0.032	0.66	0.009	0.18	0.000	0.00	0.129	2.68
	Level 3	272	4.846	0.105	2.17	0.000	0.00	0.012	0.25	0.024	0.50	0.109	2.24
NRBC#	Level 1	272	0.156	0.029	18.86	0.000	0.00	0.002	1.10	0.017	11.15	0.034	21.94
	Level 2	259	0.390	0.022	5.76	0.006	1.44	0.000	0.00	0.011	2.86	0.026	6.59
	Level 3	271	1.086	0.036	3.34	0.000	0.00	0.016	1.47	0.041	3.76	0.057	5.24

All Sites Combined				Within-Run		Between-Run		Between-Day		Between-Site		Total	
Measurand	Control Level	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
NRBC%	Level 1	272	5.321	0.546	10.26	0.000	0.00	0.072	1.36	0.071	1.33	0.555	10.44
	Level 2	260	5.421	0.304	5.60	0.038	0.70	0.000	0.00	0.033	0.61	0.308	5.68
	Level 3	272	6.304	0.210	3.33	0.000	0.00	0.085	1.34	0.040	0.64	0.230	3.65
RET#	Level 1	272	0.097	0.003	2.90	0.000	0.34	0.000	0.00	0.013	13.35	0.013	13.66
	Level 2	259	0.077	0.002	3.10	0.000	0.00	0.004	5.08	0.008	10.27	0.009	11.87
	Level 3	271	0.034	0.002	5.41	0.000	0.00	0.000	0.00	0.006	16.69	0.006	17.54
RET%	Level 1	272	4.396	0.125	2.84	0.007	0.17	0.000	0.00	0.587	13.35	0.600	13.65
	Level 2	260	1.810	0.052	2.86	0.000	0.00	0.092	5.11	0.184	10.14	0.212	11.71
	Level 3	272	0.659	0.035	5.38	0.000	0.00	0.000	0.00	0.110	16.63	0.115	17.48
IRF%	Level 1	272	36.98	2.532	6.85	1.586	4.29	4.488	12.14	5.080	13.74	7.408	20.03
	Level 2	260	33.70	2.368	7.03	1.181	3.50	4.017	11.92	4.454	13.22	6.556	19.45
	Level 3	272	23.12	2.178	9.42	0.798	3.45	1.395	6.03	2.455	10.62	3.654	15.81
IG#	Level 1	272	0.285	0.011	3.88	0.003	0.97	0.006	1.96	0.006	2.09	0.014	4.92
	Level 2	259	0.793	0.026	3.25	0.000	0.00	0.010	1.32	0.019	2.43	0.034	4.26
	Level 3	271	2.126	0.069	3.24	0.010	0.49	0.028	1.32	0.072	3.37	0.104	4.88
IG%	Level 1	272	10.23	0.370	3.62	0.051	0.50	0.141	1.37	0.035	0.34	0.400	3.92
	Level 2	260	11.04	0.315	2.85	0.043	0.39	0.103	0.94	0.000	0.00	0.334	3.03
	Level 3	272	12.34	0.385	3.12	0.014	0.11	0.116	0.94	0.000	0.00	0.403	3.26
IPF%	Level 1	271	19.03	0.583	3.06	0.000	0.00	0.170	0.89	0.000	0.00	0.607	3.19
	Level 2	260	19.98	0.673	3.37	0.000	0.00	0.309	1.55	0.000	0.00	0.741	3.71
	Level 3	271	19.90	0.677	3.40	0.000	0.00	0.369	1.85	0.114	0.57	0.779	3.91
RET-He (pg)	Level 1	271	23.70	0.140	0.59	0.059	0.25	0.051	0.22	0.619	2.61	0.640	2.70
	Level 2	260	24.96	0.175	0.70	0.083	0.33	0.230	0.92	0.469	1.88	0.557	2.23
	Level 3	272	27.16	0.370	1.36	0.000	0.00	0.116	0.43	0.891	3.28	0.972	3.58

Precision/Repeatability – Body Fluid

Repeatability (within-run precision) studies were performed to evaluate the performance of the RBC-BF parameter when diluted with CELLSHEATH(C) reagent. The studies were conducted on the XN-11, XN-21 analyzers Body Fluid Mode at three clinical sites using two high and two low residual body fluid samples for pleural, peritoneal and synovial fluids around the upper and lower limit of the analytical measuring range. Pleural, peritoneal and synovial fluids were collected in K_2EDTA anticoagulant. Each sample was run 10 consecutive times at each clinical site. The mean, standard deviation (SD), and coefficient of variation (CV) were calculated for each sample included in the study. Results of the Precision/Repeatability met the performance specifications (CV%) for the XN-Series analyzers.

Precision/Reproducibility – Body Fluid

Evaluation of body fluid reproducibility for the RBC-BF parameter which uses the CELLSHEATH(C) reagent was performed on the XN-11 and XN-21 Body Fluid Mode using two levels of quality control material (Low, and High). Each level was run in duplicate twice each day for the duration of the study or a minimum of 20 days at each of three test sites using a single control, calibration and reagent lot. All other body fluid parameters were analyzed only to show that modifications made to create the XN-11 and XN-21 analyzers does not affect the performance of all other reportable parameters. All results met the acceptance criteria for both XN-11 and XN-21. Results of XN-11 are shown below.

Body Fluid Reproducibility – Combined Sites - XN-11 Module

All Combined Sites				Within-Run		Between-Run		Between-Day		Between-Site		Total Imprecision	
Analyte	Control Level	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
WBC-BF ($x\ 10^3/\mu L$)	Level 1	244	0.081	0.003	3.87	0.002	2.79	0.004	4.88	0.007	8.49	0.009	10.89
	Level 2	244	0.315	0.007	2.34	0.000	0.00	0.005	1.74	0.026	8.28	0.028	8.78
RBC-BF ($x\ 10^6/\mu L$)	Level 1	244	0.025	0.001	3.18	0.000	0.85	0.001	2.47	0.000	0.52	0.001	4.14
	Level 2	244	0.074	0.001	1.77	0.000	0.00	0.001	1.64	0.001	2.01	0.002	3.14
TC-BF ($x\ 10^3/\mu L$)	Level 1	244	0.081	0.003	3.87	0.002	2.79	0.004	4.88	0.007	8.49	0.009	10.89
	Level 2	244	0.315	0.007	2.34	0.000	0.00	0.005	1.74	0.026	8.28	0.028	8.78
MN# ($x\ 10^3/\mu L$)	Level 1	244	0.028	0.002	7.79	0.000	0.00	0.001	3.38	0.003	10.59	0.004	13.57
	Level 2	244	0.108	0.005	4.85	0.000	0.00	0.003	2.63	0.013	12.29	0.014	13.47
PMN# ($x\ 10^3/\mu L$)	Level 1	244	0.054	0.003	5.47	0.002	3.15	0.003	6.02	0.004	7.62	0.006	11.58
	Level 2	244	0.207	0.007	3.21	0.001	0.72	0.003	1.63	0.013	6.19	0.015	7.20
MN (%)	Level 1	244	33.98	2.280	6.71	0.000	0.00	0.921	2.71	1.013	2.98	2.659	7.83
	Level 2	244	34.08	1.438	4.22	0.000	0.00	0.419	1.23	1.298	3.81	1.982	5.82
PMN (%)	Level 1	244	66.02	2.280	3.45	0.000	0.00	0.921	1.39	1.013	1.53	2.659	4.03
	Level 2	244	65.92	1.438	2.18	0.000	0.00	0.419	0.64	1.298	1.97	1.982	3.01

c. Linearity:

Whole blood

Linearity of the RBC, HGB, HCT and PLT-I parameters which uses CELLSHEATH(C) diluent was evaluated using the Linearity Kit of known concentrations of RBC, HGB and PLT which spanned the full measuring range of each of the measured parameters at three clinical sites. Linearity studies were performed according to the manufacturer's recommended procedures provided in the package insert. Linearity was demonstrated from lower limit to upper limit and within measured allowable max % diff for each interval. Results of XN-11 are shown below. XN-21 has comparable performance.

Whole Blood Linearity (Analytical Measuring Interval) – XN-11 Module

Parameter	Units	r^2	r	Slope	Intercept	Mean Replicate %Diff	Max Allowable %Diff	Range
Site 1								
RBC	$10^6/\mu L$	0.999	1.000	1.008	-0.023	0.33	±2%	0.10-8.52
HGB	g/dL	1.000	1.000	0.998	0.020	0.22	±2%	0.2-27.2
HCT	%	0.999	1.000	1.008	-0.23	1.64	±3%	1.2-76.9
PLT-I	$10^3/\mu L$	1.000	1.000	0.993	4.29	1.52	±5%	8-4917
Site 2								
RBC	$10^6/\mu L$	0.999	1.000	1.014	-0.031	1.43	±2%	0.10-8.71
XN-11 Parameter	UNITS	r^2	r	Slope	Intercept	Mean Replicate %Diff	Max Allowable %Diff	Range
HGB	g/dL	0.999	1.000	0.980	0.182	0.58	±2%	0.2-26.3
HCT	%	0.999	1.000	0.998	-0.164	0.28	±3%	1.3-81.0
PLT-I	$10^3/\mu L$	1.000	1.000	1.013	-12.52	1.15	±5%	8-4760
Site 3								
RBC	$10^6/\mu L$	0.999	1.000	0.990	0.037	1.43	±2%	0.10-8.50
HGB	g/dL	0.999	1.000	0.990	0.072	0.58	±2%	0.2-26.1
HCT	%	0.999	1.000	0.990	0.343	0.28	±3%	1.3-78.5
PLT-I	$10^3/\mu L$	1.000	1.000	0.999	-0.640	1.15	±5%	9-5127

Body Fluid

The linearity of the RBC-BF parameter which uses CELLSHEATH(C) diluent was evaluated at three clinical sites using serial dilutions of known high concentrations of body fluid samples. The samples spanned the full measuring range of the RBC-BF parameters. Pleural, peritoneal and synovial fluids were collected in K_2EDTA anticoagulant. All samples were aspirated in the body fluid mode. Each serial dilution was run in duplicate. Linearity was demonstrated from lower limit to upper limit and within measured allowable max % diff for each interval. Results for XN-11 are shown below. Similar results were obtained for XN-21.

Body Fluids Linearity - XN-11 Module

Parameter	Units	r^2	r	Slope	Intercept	Mean Replicate %Diff	Max Allowable %Diff	Range
Site 1		Pleural						
RBC-BF	x $10^6/\mu L$	1.000	1.000	0.995	0.003	0.45	±2%	0.001-6.286
Site 2		Pleural						
RBC-BF	x $10^6/\mu L$	1.000	1.000	0.987	0.009	0.293	±2%	0.001-5.220
Site 3		Pleural						
RBC-BF	x $10^6/\mu L$	0.999	1.000	1.001	-0.003	0.76	±2%	0.011-5.404

Parameter	Units	r^2	r	Slope	Intercept	Mean Replicate %Diff	Max Allowable %Diff	Range
Site 1		Synovial						
RBC-BF	x 10^6/µL	1.000	1.000	1.005	-0.001	0.73	±2%	0.002-4.178
Site 2		Synovial						
RBC-BF	x 10^6/µL	1.000	1.000	1.008	0.002	0.563	±2%	0.000-5.142
Site 3		Synovial						
RBC-BF	x 10^6/µL	1.000	1.000	1.005	-0.001	1.270	±2%	0.005-4.911

Parameter	Units	r^2	r	Slope	Intercept	Mean Replicate %Diff	Max Allowable %Diff	Range
SITE 1		Peritoneal						
RBC-BF	x 10^6/µL	1.000	1.000	1.007	-0.002	0.90	±2%	0.001-4.865
SITE 2		Peritoneal						
RBC-BF	x 10^6/µL	1.000	1.000	1.012	-0.004	0.85	±2%	0.000-5.293
SITE 3		Peritoneal						
RBC-BF	x 10^6/µL	1.000	1.000	1.002	-0.001	1.20	±2%	0.004-4.962

d. Carryover:

Whole blood

Carryover of the XN-11 and XN-21 analyzers for the directly measured RBC, HGB, HCT and PLT-I parameters which use the CELLSHEATH(C) diluent, was evaluated by assaying whole blood K_2EDTA samples with high RBC, HGB, and PLT counts three consecutive times (H1, H2, H3) followed immediately by testing samples with low target values around medical decision levels consecutively three times (L1, L2, L3). Three sets of carryover sequences were run for each type of carryover test at three clinical sites. Carryover effect was calculated for each measurand and results were within specification (≤1.0%) for WBC, RBC, HGB and PLT.

Body Fluid

Carryover of the RBC-BF parameter which uses the CELLSHEATH(C) diluent was assessed by assaying residual body fluid samples with a high RBC-BF count three consecutive times (H1, H2, H3) followed immediately by testing samples with low target values around medical decision levels consecutively three times (L1, L2, L3) in accordance with CLSI protocol H26-A2 section 5.7. Three sets of carryover sequences were run for each type of carryover test at three clinical sites. Pleural, Peritoneal and Synovial fluids were collected in K_2EDTA anticoagulant. Carryover effect was calculated for each measurand and results were within specification (≤0.3%) for WBC-BF, RBC-BF and TC-BF#.

e. Interfering Substances:

A study was conducted to determine at what level Bilirubin C interferes with the hematology results of the XN-11 and XN-21 analyzers. Six whole blood samples

from each of three donors were centrifuged and 150 µL of plasma removed from each sample tube. Bilirubin C from Interference Check A Plus (Sysmex Corp) was diluted (0%, 20%, 40%, 60%, 80%, 100%). 150 µL of each dilution was added to one of the six whole blood sample tubes. Each sample was mixed and measured three times by the whole blood mode of the instruments for RBC, HGB, HCT, and PLT-I parameters. There was no significant Bilirubin C interference up to a concentration of 40.6 mg/dL.

A study was conducted to determine at what level Bilirubin F interferes with the hematology results of the XN-11 and XN-21 analyzers. Six whole blood samples from each of three donors were centrifuged and 150 µL of plasma removed from each sample tube. Bilirubin F from Interference Check A Plus (Sysmex Corp) was diluted (0%, 20%, 40%, 60%, 80%, 100%). 150 µL of each dilution was added to one of the six whole blood sample tubes. Each sample was mixed and measured three times by the whole blood mode of the instruments for RBC, HGB, HCT, and PLT-I parameters. There was no significant Bilirubin F interference up to a concentration of 38.8 mg/dL.

A study was conducted to determine at what level Hemolytic Hemoglobin interferes with the hematology results of the XN-11 and XN-21 analyzers. Six whole blood samples from each of three donors were centrifuged and 150 µL of plasma removed from each sample tube. Bilirubin C from Interference Check A Plus (Sysmex Corp) was diluted (0%, 20%, 40%, 60%, 80%, 100%). 150 µL of each dilution was added to one of the six whole blood sample tubes. Each sample was mixed and measured three times by the whole blood mode of the instruments. Parameters tested: RBC, HGB, HCT, and PLT-I. There was no significant hemolysis interference up to a concentration of 982.0 mg/dL for RBC, HCT and PLT-I parameters and up to a concentration of 196.4 mg/dL for HGB parameter.

A study was conducted to determine at what level lipid interferes with the hematology results of the XN-11 and XN-21 analyzers. Six whole blood samples from each of three donors were centrifuged and 150 µL of plasma removed from each sample tube. Intralipid (fresenius-kabi AB) was diluted (0%, 1%, 5%, 10%, 50%, 100%). 150 µL of each dilution was added to one of the six whole blood sample tubes. Each sample was mixed and measured three times by the whole blood mode of the instruments. Parameters tested: RBC, HGB, HCT, and PLT-I. There was no significant Intralipid interference up to a concentration of 55.980 OD for RBC, HCT and PLT-I parameters. There was no significant Intralipid interference up to a concentration of 6.160 OD for HGB parameter.

A study was conducted to determine at what level Chyle interferes with the hematology results of the XN-11 and XN-21 analyzers. Six whole blood samples from each of three donors were centrifuged and 150 µL of plasma removed from each sample tube. Chyle from Inteference Check Plus (Sysmex Corp.) was diluted (0%, 20%, 40%, 60%, 80%, 100%). 150 µL of each dilution was added to one of the six whole blood sample tubes. Each sample was mixed and measured three times by the

whole blood mode of the instruments. Parameters tested: WBC, RBC, HGB, HCT, and PLT-I. There was no significant Chyle interference up to a concentration of 2820 OD for RBC, HCT and HGB parameters. There was no significant Chyle interference up to a concentration of 1128 FTU for PLT-I parameter.

2. Other Supportive Instrument Performance Data Not Covered Above:

a. Specimen Stability Studies:

Stability – Whole Blood
Whole blood stability was evaluated at one clinical site using a total of 30 (10 normal and 20 abnormal MCV) residual K_2EDTA whole blood samples on the XN-11. Twenty samples (10 normal and 10 abnormal MCV) were tested on the XN-21 due to insufficient sample volume. Two sets of samples were collected from each donor (room temperature and refrigerated). The samples were run in singlet on the XN-11 and XN-21 analyzers. Each sample was tested within 2 hours on all methods at baseline or zero (0) time, 8 hours, 24 hours, 36 hours, 48 hours and 56 hours at room temperature (RT) (18-26°C) and refrigerated temperature (LT) (2-8°C). The mean percent difference was recorded for each sample. Stability for HCT/MCV on the XN-11 and XN-21 met bias percent limits at 24 and 48 hours.

Short Term Stability– Body Fluid
Body fluid short term stability for RBC-BF parameter which uses CELLSHEATH(C) diluent was evaluated using two (2) residual Pleural, Peritoneal and Synovial fluids at Site 3. Pleural, peritoneal and synovial fluids were collected in K_2EDTA anticoagulant and run in singlet in the Body Fluid Mode. Each sample was carefully mixed by gentle hand inversion at least 10 times before analyzing on the XN-11 and XN-21 analyzers and tested at baseline (zero (0) time), 1 hour, 4 hours and 6 hours at room temperature (20-25°C). The results of the body fluid short term stability study met the acceptance bias percent limits.

b. Anticoagulant Comparison Study - K_2EDTA vs. K_3EDTA whole blood:

Anticoagulant comparison studies were performed to demonstrate comparability between K_2EDTA and K_3EDTA whole blood samples for the RBC, HGB, HCT, MCV and PLT-I parameters using the XN-Series analyzers. A total of 30 paired whole blood samples (K_2EDTA, K_3EDTA) drawn from healthy subjects were used for this study. The samples were run in singlet on the XN-11 and the results of the K_2EDTA samples were compared to the corresponding results of the K_3EDTA sample for the same donor. The results of the linear regression analysis and bias between the K_2EDTA and K_3EDTA whole blood met the acceptance criteria for all applicable parameters. This study was conducted on the XN-11 module since the data output from both the XN-11 and XN-21 is considered equal.

c. Bridging Study- Comparison of venous whole blood samples to capillary

whole blood:

A small comparison study was performed to demonstrate comparability between venous whole blood samples and capillary whole blood samples using the XN-21 analyzer. A total of 20 paired whole blood venous samples and capillary samples (K_2EDTA) drawn from healthy subjects were used for this study. The samples were run in singlet on the XN-21 and the results of the venous whole blood sample results were compared to the corresponding results of the capillary sample for the same donor. Testing was performed in the Whole Blood Manual Analysis Mode. The venous whole blood samples were placed in the Normal Tube Position of the Manual Mode and the capillary samples were placed in the Micro-collection Tube Position of the Manual Mode for analysis. Of the 20 samples tested, less than 10 samples contained NRBCs which is an insufficient number for correlation coefficient value. The results of the linear regression analysis and bias between venous whole blood samples and capillary whole blood samples on the XN-21 analyzer met the acceptance criteria for all applicable parameters.

d. Bridging Study- Comparison of K_2EDTA tubes and micro-collection tubes:

Sixty three residual K_2EDTA whole blood samples with analyte concentrations representative of normal patient samples and patient samples across clinical medical decision levels were used to determine the presence or absence of matrix effect between K_2EDTA normal tubes and micro collection tubes on the XN-11 analyzer. K_2EDTA whole blood samples were first analyzed in singlet in the Manual Mode Normal Tube Position and within two hours of analysis the samples were transferred to micro-collection tubes (without additive) and analyzed in the Manual Mode Micro-collection Tube Position. The results of the linear regression analysis and bias between the K_2EDTA tube and micro-collection tubes on the XN-11 analyzers met the acceptance criteria for all applicable parameters.

e. Bridging Study- Pre-dilute Mode Normal Tube to Micro Tube Position Comparison:

Twenty (20) residual K_2EDTA (4mL tubes) patient whole blood samples were used to determine the equivalency between the Pre-dilute Mode Normal Tube Position and the Pre-dilute Mode Micro-collection tube position. Pre-dilute (1:7) samples were prepared for each of the 20 samples by dispensing 420 µL of the analyzers diluent into plain top tubes (4mL tubes) then adding 70 µL of whole blood and mixing 10 times by gentle inversion. The plain top 4mL tubes were analyzed in singlet on the XN-21 analyzer within 1 hour of dilution preparation in the Pre-dilute Mode normal tube position. Immediately following, the samples were mixed 10 times then transferred to micro-collection tubes (without additive) and analyzed in the Pre-dilute Mode Micro-collection tube position (Cap Off). The pre-dilute mode automatically multiplies sample results by 7 before results are displayed therefore no additional calculation is required. The results of the linear regression analysis

and bias between the Pre-dilute Mode normal tube and Pre-dilute mode micro-collection tube on the XN-21 analyzer met the acceptance criteria in the Pre-dilute Mode for all applicable parameters.

f. Bridging Study- Low WBC Mode Normal Tube to Micro Tube Position Comparison:

Forty (40) residual K_2EDTA anticoagulated whole blood patient samples were selected to determine the equivalency between the Low WBC Mode normal tube position and the Low WBC Mode micro-collection tube position. The patients original K_2EDTA tube was mixed by gentle hand inversion 10 times and run in singlet in the Low WBC Mode Normal Tube Position on the XN-21 analyzer. The samples were then transferred to micro-collection tubes (without additive), mixed 8-10 times before running in the Low WBC Mode Micro-collection Tube Position (Cap Off) on the XN-21 analyzer within 1 hour of analysis of the Low WBC Mode Normal Tube Position. The results of the linear regression analysis and bias between the Low WBC Mode normal tube position and Low WBC Mode micro-collection tube position met the acceptance criteria for the Low WBC Mode for all applicable parameters.

g. Determination of limit of blank, lower limits of detection and quantitation:

Verification of Limit of Blank (LoB)
Verification of the Limit of Blank (LoB) was obtained from 40 repeated measurements of one blank sample (CELLPACK) on the XN-11 module. Testing was performed by one operator in the appropriate sampling mode for whole blood and body fluid mode for body fluids. The Mean, SD and Limit of Blank were calculated for the RBC, HCT, HGB, PLT-I, and RBC-BF parameters. The estimated LoB equals the 95^{th} percentile of the distribution of blank values. The LoB for both the XN-11 and XN-21 analyzers for whole blood parameters RBC, HGB, HCT, PLT-I and the body fluid RBC-BF is zero (0) cells/µL.

Verification of the Limit of Detection (LoD)
Verification of the Limit of Detection was obtained from 40 repeated measurements of two low concentration samples over a two day period (1 sample each day) on the XN-11 module. Two whole blood K_2EDTA samples and two body fluid samples (pleural and peritoneal) were diluted using instrument diluent to achieve low cell concentrations with target values of $0.02 – 0.06 \times 10^6$/µL for RBC (HGB,HCT), $1 – 3 \times 10^3$/µL for PLT-I and $0.003 – 0.005 \times 10^6$/µL for RBC-BF parameters. Testing was performed by one operator in the appropriate sampling mode for whole blood and body fluid mode for body fluids. The mean, SD and LoD were calculated for the RBC, HGB, HCT, PLT-I and RBC-BF parameters.

Verification of the Limit of Quantitation (LoQ)
Verification of the Limit of Quantitation was obtained by using the test results from the LoD study to determine the bias and imprecision for that level of analyte. Forty replicate measurements (one sample) of the lowest measured concentration for each analyte were performed on the XN-11 module to verify precision at the low end of the analytical measuring range. The mean, SD and

2SD were calculated for the RBC, HGB, HCT, PLT-I and RBC-BF parameters to verify precision at the lower end of the measuring range for each parameter.

The results of the LoB, LoD and LoQ meet the manufacturer's expected performance for background limits and the lower limit of the measuring range for RBC, HGB, HCT and PLT-I.

h. SP-10 automated slide stainer

i. Verification of Method Comparison Using Whole Blood with the addition of the SP-10 automated slide stainer:

Verification of comparability of whole blood on the XN-Series analyzer when connected to the SP-10 automated slide preparation and staining unit were performed by comparing the data from a configuration consisting of two (2) XN-11 analyzers connected to one another and a SP-10 unit was compared with data from a standalone XN-21 analyzer (not connected to a SP-10). Samples included normal healthy donors and abnormal samples with a variety of hematological conditions and spanned the analytical measuring range. Samples were analyzed first on the standalone XN-21 analyzer in the Whole Blood Sampling Mode. Within 2 hours of analysis on the standalone XN-21 analyzer, whole blood samples were analyzed on the XN-11 analyzer that is connected to the SP-10 unit. The XN-11/XN-21 analyzers performed within the manufacturer's specifications when connected to the SP-10.

ii. Verification of XN-Series Body Fluid Performance when connected to the SP-10 automated stainer:

A small method comparison study was performed to verify performance claims for the XN-11 and XN-21 analyzers are met when connected to each other and a SP-10 unit. Samples used in this study covered the full reportable measuring ranges to the extent possible of the XN-Series analyzers. All samples were collected in K_2EDTA anticoagulant. Sample concentrations and dilutions were also used when native samples representing the full reportable range of WBC-BF and RBC-BF parameters were not available. Data from a configuration consisting of two XN-11 analyzers connected to one another and a SP-10 unit was compared with data from a standalone XN-21 analyzer (not connected to a SP-10). The XN-11/XN-21 analyzers performed within the manufacturer's specifications when connected to the SP-10.

iii. Determination of Limit of Blank (LoB), Lower Limits of Detection (LoD) and Quantitation (LoQ) when connected to the SP-10:

<u>Verification of Limit of Blank (LoB)</u>
Verification of the Limit of Blank (LoB) was obtained from 40 repeated measurements of one blank sample (CELLPACK) on the XN-11 module. Testing was performed by one operator in the appropriate sampling mode

for whole blood. The mean, SD and LoB were calculated for the RBC, HCT, HGB and PLT-I parameters.

Verification of the Limit of Detection (LoD) and Limit of Quantitation (LoQ)

The manufacturer's lower bound analytical range for WBC, RBC, HGB, HCT and PLT parameters were selected as target values to verify the LoD and LoQ for these parameters. Forty replicate measurements (one sample) of the lowest measured concentration for each analyte were performed in the whole blood mode on the XN-11 module to verify precision at the low end of the analytical measuring range. The mean, SD and 2SD were calculated for the WBC, RBC, HGB, HCT and PLT to verify precision at the lower end of the measuring range for each parameter.
The results of the whole blood LoB, LoD and LoQ for the XN-11 module met the manufacturer's performance claims for the WBC, RBC, HGB, HCT and PLT parameters.

iv. SP-10 Functionality - Slides for Positive Specimens

The ability of the SP-10 when connected to two XN-Series analyzers to appropriately read sample barcode identification labels, receive sample judgment results (Negative/Positive) and generate blood smears was conducted using 50 de-identified residual whole blood samples. Sample flagging (Negative/Positive) results generated from the XN-Series analyzers were compared to the number of slides produced by the SP-10 (produced for positive/abnormal samples) and slides not produced by the SP-10 (not produced for negative/normal samples). Slides were divided into two categories: (1) P - slide was made for a Positive sample, and (2) N - no slide was made for a Negative sample. Slides for positive Specimens Analysis results met pre-defined acceptance criteria of the number of samples flagged as Positive (abnormal) and the number of slides produced from the SP-10 will have an Overall Agreement of ≥90%. The SP-10 will not produce slides from samples flagged as Negative (normal) by the XN analyzers.

i. Reference Intervals:

Verification of Adult Reference Intervals

Adult Reference intervals (normal population reference ranges) were assessed for the XN-11 and XN- 21 series analyzers by comparing normal K_2EDTA anticoagulated samples collected from normal male and female donors >21 years of age. Pre-established reference intervals from the XE-5000 predicate device were used as a default normal range flag. The study results showed that less than 10 percent of samples tested were outside the proposed reference intervals.

Due to the unavailability of obtaining normal body fluid samples, it is difficult for laboratories to establish reference intervals; therefore, Sysmex

recommends that laboratories reference textbook values for their body fluid reference intervals.

Sysmex recommends that each laboratory establishes its own expected reference intervals based upon the laboratory's patient population encountered during daily operation. Expected reference intervals may vary due to the differences in sex, age, diet, fluid intake, geographic location.

K. Proposed Labeling:

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

L. Conclusion:

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