510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k112605

B. Purpose for Submission:

New device

C. Manufacturer and Instrument Name:

Sysmex America, Inc.; Sysmex® XN-Series (XN-10, XN-20) Automated Hematology Analyzers

D. Type of Test or Tests Performed:

Quantitative test for 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, WBC-BF, RBC-BF, MN%/#, PMN%/#, and TC-BF parameters

E. System Descriptions:

1. Device Description:
   The Sysmex® XN-Series modules (XN-10, XN-20) are multi-parameter hematology analyzers intended to perform tests on whole blood samples collected in K_2 or K_3EDTA and body fluids (pleural, peritoneal and synovial) collected in K_2EDTA anticoagulant. The analyzers can also perform tests on CSF which should not be collected in any anticoagulant. The XN-Series modules consist of four principal units: (1) Two Main Units (XN-10, XN-20) which aspirate, dilute, mix, and analyze blood and body fluid samples; (2) Two Auto Sampler Units (SA-10, SA-20) 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.

   Three configurations for the XN-Series modules are provided:

   a. XN-1000 comprised of:
      1) XN-10
      2) XN-20
      3) SA-10 (Auto Sampler for single module)

   b. XN-2000 comprised of:
      1) Two XN-10 or XN-20 or combination
      2) SA-20 (Auto Sampler for two modules)

   c. XN-9000 comprised of:
      1) One to nine XN-10 or XN-20 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: Radio-frequency (RF) / Direct-current (DC) Detection Method, Sheath Flow DC Detection Method, and Flow Cytometry Methods using a Semiconductor Laser and Sodium Lauryl Sulfate (SLS)-hemoglobin. Particle characterization and identification is based on detection of forward scatter, fluorescence and adaptive cluster analysis. The XN-Series analyzers automatically classify cells from whole blood and body fluids and carry out all processes automatically from aspiration of the sample to outputting the results.

The body fluid analysis mode of the XN-Series analyzers uses the 4DIFF scattergram & 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 & 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:
Sampler Analysis Mode
Manual (Closed and Open Cap) Analysis Modes
Pre-dilute Analysis Mode (Dilute sample 1:7)
Low WBC Mode (LWBC)
Body Fluid Analysis Mode

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. 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.

6. Calibration:
XN CAL™ is used for calibration of the instrument for WBC, RBC, HGB, HCT, PLT and RET. XN CAL PF™ 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 the QC data is fluctuating) to ensure accuracy of the system.

7. Quality Control:

The XN CHECK™ whole blood quality control material (three levels) and the XN BF CHECK™ 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:

1. Indication(s) for Use:
   The XN-Series modules (XN-10, XN-20) are quantitative multi-parameter automated hematology analyzers intended for in vitro diagnostic use in screening patient populations found in clinical laboratories.

   The XN-Series modules classify and enumerate the following parameters in whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, IG%/#, RDW-CV, RDW-SD, MPV, NRBC#/%, RET%/#, IPF, IRF, RET-He and has a Body Fluid mode for body fluids. The Body Fluid mode enumerates the WBC-BF, RBC-BF, MN%/#, PMN%/#, and TC-BF parameters in cerebrospinal fluid (CSF), serous fluids (peritoneal, pleural) and synovial fluids. Whole blood should be collected in K_2 or K_3EDTA anticoagulant and, Serous and Synovial fluids in K_2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with CSF specimens is neither required nor recommended.

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-10, XN-20)	Predicate: XE-5000
Intended Use	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, 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 K_2 or K_3EDTA anticoagulant and, Serous and Synovial fluids in K_2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with CSF specimens is neither required nor recommended.	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 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
Modes of Operation	Sampler Analysis Mode Manual Closed Analysis Mode Body Fluid Analysis Mode	Same
Measuring Channels	RET/PLT	Same

Differences		
Item	Device: XN-Series (XN-10, XN-20)	Predicate: XE-5000
Controls/ Calibrators	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	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
Sample Type	Not Available	Umbilical Cord Blood
Parameters	Not Available	HPC
Sample Aspiration/ Fluidic Pathway	Single pathway	Two pathways
Software/Hardware	Rules-based rerun / reflex	No Rules-based rerun / reflex
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 in XN-10) PLT-F	WBC/BASO, DIFF, NRBC, IMI Not Available
Reagents	CELLPACKTM DCL (Diluent) CELLPACKTM DFL (Diluent) LYSERCELL WNR (Lyse) LYSERCELL WDF (Lyse) LYSERCELL WPC (Lyse) FLUOROCELL WNR (Stain) FLUOROCELL WDF (Stain) FLUOROCELL RET (Stain) FLUOROCELL PLT (Stain) FLUOROCELL WPC (Stain)	CELLPACK™ (Diluent) CELLSHEATH™ (Diluent) Stromatolyser-FB™ (Lyse) Stromatolyser -4DL™ (Lyse) Stromatolyser - IM™ (Lyse) Stromatolyser -4DS™ (Stain) Stromatolyser -NR™ (Diluent) Stromatolyser -NR™ (Stain) RET-SEARCH II (Diluent) RET-SEARCH II (Stain)
Sample Aspiration Volume	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	Sampler Mode – 200 µL Manual (Closed Cap) Mode-200 µL Manual (Open Cap) Mode – 130 µL Capillary Mode – 130 µL Body Fluid Mode – 130 µL

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

Class II Special Controls Guidance Document: Premarket Notifications for Automated Differential Cell Counters for Immature or Abnormal Blood Cells; Final Guidance for Industry and FDA

CLSI 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

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

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 assess the performance of the XN-Series (XN-10, XN-20) analyzers when compared to the XE-5000 analyzer using a total of 304 residual clinical K_2 EDTA whole blood samples at three US sites. All samples were run in the Automated Sampling Modes in singlet on the XE-5000 and within two hours on the XN-Series analyzers. Samples covered clinical medical decision levels, and of the full reportable measuring ranges of the XN-Series analyzers. The results of the linear regression and bias analyses between the XE-5000 and XN-Series Whole Blood Mode met the acceptance criteria for all applicable parameters for correlation coefficient (r) and %Bias with the exception of RET-He which has a slightly lower r value on the XN-10 (r=0.88); however, the %Bias was within the acceptable %Bias Limits and the reticulocyte parameter from which the RET-He is derived met the acceptance criteria. An example of the

results between XN-10 and XE-5000 is shown below and comparable results are obtained with the XN-20.

Correlation and Estimated Bias (Whole Blood - combined sites): (XE-5000 vs. XN-10)

Measurand	N	Result Range	r	Slope (95% CI)	Intercept (95% CI)	Mean Diff	Mean %Diff
WBC ($10^3/\mu L$)	304	1.37-112.96	0.9992	0.951 (0.947, 0.956)	0.291 (0.235, 0.347)	0.18	1.90
RBC ($10^6/\mu L$)	304	1.69-7.25	0.9983	1.059 (1.052, 1.066)	-0.261 (-0.291, -0.232)	-0.01	0.46
HGB (g/dL)	304	5.1-23.3	0.9986	1.007 (1.001, 1.013)	-0.09 (-0.16, -0.01)	-0.0	0.1
HCT (%)	304	15.5-68.8	0.9971	1.045 (1.036, 1.054)	-1.84 (-2.19, -1.50)	-0.2	0.5
MCV (fL)	304	66.2-108.5	0.9911	1.009 (0.994, 1.024)	-0.82 (-2.19, 0.54)	0.03	0.03
MCH (pg)	304	20.6-35.4	0.9681	1.024 (0.995, 1.054)	-0.39 (-1.25, 0.48)	N/A	N/A
MCHC (g/dL)	304	29.00-36.00	0.8993	0.961 (0.912, 1.010)	1.667 (0.050, 3.284)	N/A	N/A
PLT-I ($10^3/\mu L$)	304	20-3109	0.9960	1.027 (1.016, 1.037)	0.1 (-3.5, 3.8)	-6.0	2.6
RDWSD (fL)	304	34.7-75.9	0.9931	1.027 (1.013, 1.041)	-2.48 (-3.13, -1.83)	1.2	-2.5
RDWCV (%)	304	11.8-23.3	0.9918	1.052 (1.036, 1.067)	-1.14 (-1.36, -0.91)	0.3	-2.6
MPV (fL)	304	8.6-14.4	0.9219	1.024 (0.978, 1.070)	-0.09 (-0.59, 0.41)	0.1	1.54
NEUT%	304	1.0-98.1	0.9971	0.990 (0.982, 0.999)	1.40 (0.84, 1.95)	0.01	-1.24
LYMPH%	304	1.2-97.8	0.9957	0.986 (0.976, 0.996)	-0.67 (-0.97, -0.37)	-0.04	4.23
MONO%	304	0.0-33.9	0.9638	0.962 (0.933, 0.992)	0.39 (0.11, 0.67)	0.008	-0.8
EO%	304	0.0-42.0	0.9951	0.961 (0.950, 0.972)	0.03 (-0.02, 0.08)	-0.04	2.45
BASO%	304	0.0-3.7	0.8039	1.134 (1.055, 1.214)	0.17 (0.13, 0.22)	0.34	-34.3
IG%	304	0.0-25.3	0.9641	1.121 (1.087, 1.155)	0.29 (0.18, 0.39)	0.27	-27.63
NRBC# ($10^3/\mu L$)	304	0.00-11.39	0.9915	0.809 (0.797, 0.821)	0.011 (0.003, 0.019)	N/A	N/A
NRBC%	304	0.0-38.4	0.9943	0.833 (0.823, 0.843)	0.08 (0.06, 0.11)	-0.09	-8.82
RET# ($10^6/\mu L$)	304	0.0039-0.3228	0.9419	1.064 (1.023, 1.105)	0.00062 (-0.00272, 0.00396)	N/A	N/A
RET%	304	0.10-13.12	0.9778	0.972 (0.949, 0.995)	0.125 (0.069, 0.181)	0.07	3.92
IRF (%)	304	0.0-50.3	0.9506	0.968 (0.934, 1.003)	0.45 (-0.13, 1.04)	0.02	0.14
RET-HE (pg)	304	14.7-40.7	0.8828	1.021 (0.965, 1.077)	-0.27 (-2.08, 1.54)	0.4	1.22
IPF (%)	304	0.8-17.8	0.8576	0.923 (0.867, 0.979)	-0.08 (-0.36, 0.20)	0.3	-9.4
PLT-F ($10^3/\mu L$)	304	19-3268	0.9952	0.949 (0.938, 0.959)	15.2 (11.4, 19.0)	1.2	0.4

Body fluid

Method comparison studies were performed to assess the performance of the XN-series (XN-10, XN-20) Body Fluid Mode when compared to the XE-5000 analyzer using a total of 309 residual body fluid samples at three US sites. All body fluids (peritoneal, pleural, and synovial) were collected in K_2EDTA anticoagulant with exception of CSF. All samples were run in the Body Fluid Mode in singlet on the

XE-5000 and within two hours on the XN-series analyzers. Samples covered clinical medical decision levels, and of the full reportable measuring ranges of the XN-series analyzers. All body fluids tested on XN-10 and XN-20 modules showed good correlation when compared to the XE-5000. The estimation of the bias of the body fluids collected met the bias limits. Shown below are comparison results for XN-10. Similar results were obtained for XN-20.

Correlation and Estimated Bias (Body Fluids - combined sites): (XE-5000 vs. XN-10)

Fluid Type	Measurand	N	Result Range	r	Slope (95% CI)	Intercept (95% CI)	Mean Difference	%Difference or SD
CSF	WBC-BF $10^3/\mu L$	93	0.000-10.039	0.9971	0.992 (0.976, 1.008)	-0.0023 (-0.0450, 0.0405)	0.052	-3.1
	TC-BF $10^3/\mu L$	93	0.000-5.269	0.9997	1.018 (1.012, 1.023)	-0.0027 (-0.0097, 0.0044)	0.048	-2.7
	RBC-BF $10^6/\mu L$	93	0.000-10.048	0.9970	0.991 (0.976, 1.007)	-0.0025 (-0.0452, 0.0403)	0.004	0.8
	PMN# $10^3/\mu L$	93	0.000-7.358	0.9938	0.975 (0.953, 0.998)	0.0030 (-0.0274, 0.0334)	0.033	1SD
	PMN%	93	0.000-8.719	0.9980	1.031 (1.018, 1.045)	-0.0246 (-0.0481, -0.0012)	0.0	1SD
	MN# $10^3/\mu L$	93	0.0-100.0	0.9637	0.981 (0.926, 1.036)	1.21 (-0.70, 3.12)	0.039	1SD
	MN%	93	0.0-100.0	0.9702	0.981 (0.931, 1.031)	0.64 (-3.00, 4.29)	0.0	1SD
Pleural	WBC-BF $10^3/\mu L$	87	0.010-10.009	0.9988	1.011 (1.000, 1.021)	-0.0165 (-0.0433, 0.0103)	0.001	-0.4
	TC-BF $10^3/\mu L$	87	0.000-2.500	0.9983	1.006 (0.993, 1.019)	-0.0064 (-0.0135, 0.0007)	0.007	0.5
	RBC-BF $10^6/\mu L$	87	0.010-10.043	0.9987	1.011 (0.999, 1.022)	-0.0080 (-0.0370, 0.0210)	0.004	-1.5
	PMN# $10^3/\mu L$	87	0.002-4.313	0.9986	1.069 (1.057, 1.081)	-0.0153 (-0.0255, 0.0051)	0.017	1SD
	PMN%	87	0.006-7.525	0.9989	0.987 (0.977, 0.997)	-0.0049 (-0.0241, 0.0143)	0.6	1SD
	MN# $10^3/\mu L$	87	8.7-98.3	0.9804	1.023 (0.979, 1.066)	-0.26 (-2.32, 1.81)	0.016	1SD
	MN%	87	1.7-91.3	0.9803	1.023 (0.979, 1.067)	-2.02 (-4.79, 0.74)	0.6	1SD
Peritoneal	WBC-BF $10^3/\mu L$	72	0.006-10.470	0.9938	1.004 (0.977, 1.030)	0.0127 (-0.0429, 0.0683)	0.016	1.5
	TC-BF $10^3/\mu L$	72	0.000-4.698	0.9992	1.000 (0.991, 1.010)	-0.0018 -0.0117, 0.0082)	0.023	2.5
	RBC-BF $10^6/\mu L$	72	0.004-10.474	0.9915	0.995 (0.964, 1.026)	0.0279 (-0.0305, 0.0862)	0.001	0.4
	PMN# $10^3/\mu L$	72	0.003-6.862	0.9918	1.020 (0.989, 1.051)	-0.0057 (-0.0457, 0.0343)	0.014	1SD
	PMN%	72	0.003-7.851	0.9982	1.033 (1.019, 1.048)	-0.0059 (-0.0281, 0.0163)	2.5	1SD
	MN# $10^3/\mu L$	72	5.4-97.7	0.9898	1.053 (1.017, 1.089)	-0.22 (-2.34, 1.90)	0.005	1SD
	MN%	72	2.3-94.6	0.9898	1.053 (1.017, 1.089)	-5.11 (-7.08, 3.15)	2.5	1SD
Synovial	WBC-BF $10^3/\mu L$	57	0.102-10.699	0.9965	0.958 (0.936, 0.980)	0.0209 (-0.0427, 0.0845)	0.052	-3.0
	TC-BF $10^3/\mu L$	57	0.000-5.888	0.9998	1.010 (1.005, 1.016)	-0.0009 (-0.0083, 0.0064)	0.048	-2.7
	RBC-BF $10^6/\mu L$	57	0.102-10.700	0.9964	0.958 (0.936, 0.980)	0.0259 (-0.0384, 0.0902)	0.004	0.8

Fluid Type	Measurand	N	Result Range	r	Slope (95% CI)	Intercept (95% CI)	Mean Difference	%Difference or SD
	PMN# $10^3/\mu L$	57	0.032-3.718	0.9756	0.865 (0.813, 0.917)	0.0480 (-0.0059, 0.1018)	0.013	1SD
	PMN%	57	0.023-8.042	0.9979	0.983 (0.965, 1000)	0.0060 (-0.0314, 0.0435)	0.0	1SD
	MN# $10^3/\mu L$	57	4.4-97.6	0.9533	1.018 (0.934, 1.103)	-0.87 (-4.75, 3.01)	0.039	1SD
	MN%	57	2.4-95.6	0.9533	1.018 (0.934, 1.103)	-0.98 (-6.15, 4.19)	0.0	1SD

Flagging capabilities

Clinical sensitivity/specificity studies were conducted to evaluate the flagging capabilities of the XN-Series using patient samples representing a variety of abnormal conditions in comparison to the XE-5000. The results of the XN-Series 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.

Overall Flagging Analysis (combined sites): Xe-5000 vs. XN-10

		XE-5000		
		Positive (Abnormal)	Negative (Normal)	Total
XN-10	Positive (Abnormal)	147	8	155
	Negative (Normal)	10	139	149
	Total	157	147	304

% Positive Agreement = 147/(147 + 10) x 100% = 93.6%
% Negative Agreement = 139/(139 + 8) x 100% = 94.6%
% Overall Agreement = (147+139)/304 x 100% = 94.1%

Overall Flagging Analysis (combined sites): XE-5000 vs. XN-20

		XE-5000		
		Positive (Abnormal)	Negative (Normal)	Total
XN-20	Positive (Abnormal)	148	9	157
	Negative (Normal)	9	138	147
	Total	157	147	304

% Positive Agreement = 148/(148 + 9) x 100% = 94.3%
% Negative Agreement = 138/(138 + 9) x 100% = 93.9%
% Overall Agreement = (148 + 138)/304 x 100% = 94.1%

b. Precision/Reproducibility:

Precision/Repeatability Study – Whole Blood Mode

Within-run precision studies were performed 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

Precision/Reproducibility studies were performed on the XN-Series analyzers (XN-10, XN-20) Whole Blood Manual Mode using three levels of quality control material (Low, Normal and High). Each level was run in duplicate twice each day for a minimum of 25 days using a single control lot at each of the three test sites. The results of the whole blood precision (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-10 and XN-20 have similar results and met the acceptance criteria. Table below summarizes results from XN-10.

Whole Blood Reproducibility (Combined Sites)

XN-10 Module													
Measurand	Control Level	N	Mean	Within-run		Between-run		Between-day		Between-site		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
WBC ($10^3/\mu L$)	Low	364	2.852	0.058	2.03	0.022	0.77	0.023	0.81	0.02	0.70	0.069	2.42
	Normal	369	6.447	0.088	1.36	0.034	0.53	0.035	0.54	0.06	0.93	0.117	1.82
	High	362	16.793	0.159	0.95	0.097	0.58	0.037	0.22	0.01	0.06	0.190	1.13
RBC ($10^6/\mu L$)	Low	364	2.271	0.021	0.92	0.000	0.00	0.008	0.35	0.01	0.44	0.025	1.08
	Normal	369	4.428	0.030	0.68	0.004	0.09	0.015	0.34	0.01	0.23	0.035	0.8
	High	362	5.324	0.034	0.64	0.006	0.11	0.029	0.54	0.05	0.94	0.067	1.26
HGB (g/dL)	Low	364	6.5	0.050	0.77	0.040	0.62	0.020	0.31	0.02	0.31	0.070	1.08
	Normal	369	13.49	0.070	0.52	0.020	0.15	0.040	0.30	0.01	0.07	0.084	0.62
	High	362	17.3	0.080	0.46	0.010	0.06	0.070	0.40	0.11	0.64	0.153	0.89
HCT (%)	Low	364	18.51	0.210	1.13	0.070	0.38	0.170	0.92	0.11	0.59	0.300	1.62
	Normal	369	38.37	0.380	0.99	0.080	0.21	0.410	1.07	0.01	0.03	0.565	1.47
	High	362	48.64	0.420	0.86	0.290	0.60	0.440	0.90	1.23	2.53	1.402	2.88
MCV (fL)	Low	364	81.51	0.470	0.58	0.360	0.44	0.720	0.88	0.59	0.72	1.103	1.35
	Normal	369	86.67	0.520	0.60	0.320	0.37	0.880	1.02	0.29	0.33	1.110	1.28
	High	362	91.37	0.570	0.62	0.550	0.60	0.750	0.82	1.82	1.99	2.122	2.32
MCH (pg)	Low	364	28.59	0.280	0.98	0.190	0.66	0.130	0.45	0.11	0.38	0.379	1.32
	Normal	369	30.46	0.270	0.89	0.000	0.00	0.150	0.49	0.05	0.16	0.313	1.03
	High	362	32.5	0.260	0.80	0.090	0.28	0.180	0.55	0.09	0.28	0.341	1.05
MCHC (g/dL)	Low	364	35.09	0.400	1.14	0.170	0.48	0.350	1.00	0.32	0.91	0.643	1.83
	Normal	369	35.16	0.390	1.11	0.070	0.20	0.420	1.19	0.07	0.20	0.582	1.65
	High	362	35.57	0.340	0.96	0.230	0.65	0.390	1.10	0.7	1.97	0.900	2.53
PLT-I ($10^3/\mu L$)	Low	364	50.4	1.400	2.78	1.300	2.58	1.500	2.98	1.87	3.71	3.065	6.08
	Normal	369	216.8	4.500	2.08	1.900	0.88	2.800	1.29	0.02	0.01	5.630	2.6
	High	362	515.5	8.100	1.57	0.000	0.00	4.800	0.93	8.3	1.61	12.551	2.43
PLT-F ($10^3/\mu L$)	Low	364	48.5	1.100	2.27	0.900	1.86	1.400	2.89	1.24	2.56	2.349	4.84
	Normal	369	237.6	4.500	1.89	3.600	1.52	20.500	8.63	4.96	2.09	21.865	9.2
	High	362	592	9.900	1.67	6.700	1.13	24.800	4.19	21.29	3.60	34.802	5.88
RDW-SD (fL)	Low	364	43.16	0.340	0.79	0.220	0.51	0.290	0.67	0.28	0.65	0.571	1.32
	Normal	369	44.02	0.370	0.84	0.280	0.64	0.600	1.36	0.23	0.52	0.793	1.8
	High	362	44.97	0.340	0.76	0.400	0.89	0.750	1.67	0.51	1.13	1.048	2.33
RDW-CV (%)	Low	364	14.73	0.130	0.88	0.110	0.75	0.050	0.34	0.05	0.34	0.184	1.25
	Normal	369	14.1	0.080	0.57	0.010	0.07	0.040	0.28	0.01	0.07	0.091	0.64
	High	362	13.67	0.070	0.51	0.040	0.29	0.070	0.51	0.03	0.22	0.111	0.81
MPV (fL)	Low	364	9	0.230	2.56	0.080	0.89	0.130	1.44	0.14	1.56	0.310	3.44
	Normal	369	9.54	0.100	1.05	0.000	0.00	0.080	0.84	0.02	0.21	0.130	1.36
	High	362	9.39	0.060	0.64	0.020	0.21	0.080	0.85	0.09	0.96	0.136	1.45
NEUT# ($10^3/\mu L$)	Low	364	1.12	0.038	3.39	0.016	1.43	0.000	0.00	0.01	0.89	0.0424	3.79
	Normal	369	2.83	0.074	2.61	0.007	0.25	0.015	0.53	0.02	0.71	0.0784	2.77

XN-10 Module													
Measurand	Control Level	N	Mean	Within-run		Between-run		Between-day		Between-site		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
	High	362	8.087	0.173	2.14	0.031	0.38	0.034	0.42	0.04	0.49	0.1834	2.27
NEUT%	Low	364	39.26	1.090	2.78	0.470	1.20	0.000	0.00	0.07	0.18	1.189	3.03
	Normal	369	43.9	0.990	2.26	0.000	0.00	0.270	0.62	0.05	0.11	1.027	2.34
	High	362	48.15	0.970	2.01	0.000	0.00	0.260	0.54	0.25	0.52	1.035	2.15
LYMPH# ($10^3/\mu L$)	Low	364	0.969	0.043	4.44	0.022	2.27	0.000	0.00	0.01	1.03	0.0493	5.09
	Normal	369	1.858	0.075	4.04	0.048	2.58	0.000	0.00	0	0.00	0.0890	4.79
	High	362	3.547	0.132	3.72	0.046	1.30	0.000	0.00	0.03	0.85	0.1430	4.03
LYMPH%	Low	364	34.02	1.310	3.85	0.560	1.65	0.000	0.00	0.05	0.15	1.426	4.19
	Normal	369	28.82	1.140	3.96	0.650	2.26	0.000	0.00	0.33	1.15	1.353	4.7
	High	362	21.15	0.830	3.92	0.180	0.85	0.180	0.85	0.19	0.90	0.889	4.2
MONO# ($10^3/\mu L$)	Low	364	0.356	0.034	9.55	0.000	0.00	0.010	2.81	0.01	2.81	0.0368	10.34
	Normal	369	0.771	0.070	9.08	0.032	4.15	0.012	1.56	0.03	3.89	0.0835	10.83
	High	362	2.411	0.136	5.64	0.038	1.58	0.011	0.46	0.05	2.07	0.1502	6.23
MONO%	Low	364	12.47	1.160	9.30	0.000	0.00	0.300	2.41	0.13	1.04	1.205	9.66
	Normal	369	11.95	1.070	8.95	0.520	4.35	0.000	0.00	0.4	3.35	1.255	10.5
	High	362	14.34	0.830	5.79	0.080	0.56	0.090	0.63	0.28	1.95	0.884	6.17
EO# ($10^3/\mu L$)	Low	364	0.272	0.022	8.09	0.000	0.00	0.004	1.47	0.00	0.00	0.0224	8.22
	Normal	369	0.679	0.055	8.10	0.000	0.00	0.012	1.77	0.01	1.47	0.0572	8.42
	High	362	1.937	0.139	7.18	0.000	0.00	0.037	1.91	0.03	1.55	0.1469	7.59
EO%	Low	364	9.53	0.760	7.97	0.000	0.00	0.000	0.00	0.03	0.31	0.761	7.98
	Normal	369	10.53	0.830	7.88	0.000	0.00	0.110	1.04	0.02	0.19	0.837	7.95
	High	362	11.52	0.830	7.20	0.110	0.95	0.150	1.30	0.15	1.30	0.864	7.5
BASO# ($10^3/\mu L$)	Low	364	0.136	0.006	4.41	0.002	1.47	0.001	0.74	0.00	0.00	0.0064	4.71
	Normal	369	0.309	0.009	2.91	0.002	0.65	0.002	0.65	0.00	0.00	0.0094	3.05
	High	362	0.811	0.017	2.10	0.009	1.11	0.002	0.25	0.00	0.00	0.0193	2.38
BASO%	Low	364	4.76	0.180	3.78	0.000	0.00	0.020	0.42	0.01	0.21	0.181	3.81
	Normal	369	4.8	0.130	2.71	0.000	0.00	0.000	0.00	0.01	0.21	0.130	2.72
	High	362	4.83	0.100	2.07	0.040	0.83	0.000	0.00	0.02	0.41	0.110	2.27
NRBC# ($10^3/\mu L$)	Low	364	0.132	0.012	9.09	0.005	3.79	0.000	0.00	0.00	0.00	0.0130	9.85
	Normal	369	0.376	0.020	5.32	0.005	1.33	0.004	1.06	0.00	0.00	0.0210	5.59
	High	362	0.978	0.037	3.78	0.000	0.00	0.012	1.23	0.00	0.00	0.0389	3.98
NRBC%	Low	364	4.62	0.410	8.87	0.160	3.46	0.000	0.00	0.09	1.95	0.449	9.72
	Normal	369	5.84	0.320	5.48	0.070	1.20	0.070	1.20	0.00	0.00	0.335	5.74
	High	362	5.83	0.230	3.95	0.000	0.00	0.060	1.03	0.01	0.17	0.238	4.08
RET# ($10^6/\mu L$)	Low	364	0.14386	0.004	2.69	0.003	1.91	0.011	7.81	0.01	6.95	0.01578	10.97
	Normal	369	0.0953	0.003	3.41	0.002	2.52	0.007	7.81	0.00	0.00	0.00847	8.88
	High	362	0.0392	0.002	5.18	0.001	2.12	0.004	9.69	0.00	0.00	0.00439	11.19
RET%	Low	364	6.339	0.176	2.78	0.137	2.16	0.498	7.86	0.5	7.89	0.740	11.68
	Normal	369	2.156	0.079	3.66	0.052	2.41	0.169	7.84	0.01	0.46	0.194	8.99
	High	362	0.742	0.046	6.20	0.012	1.62	0.072	9.70	0.07	9.43	0.111	14.97
IRF%	Low	364	42.72	4.400	10.30	2.490	5.83	4.110	9.62	3.81	8.92	7.548	17.67
	Normal	369	47.86	4.050	8.46	0.630	1.32	3.370	7.04	0.76	1.59	5.360	11.2
	High	362	30.03	2.810	9.36	1.560	5.19	0.880	2.93	0.7	2.33	3.405	11.34
IG# ($10^3/\mu L$)	Low	364	0.287	0.012	4.18	0.004	1.39	0.003	1.05	0.00	0.00	0.0130	4.53
	Normal	369	0.71	0.030	4.23	0.000	0.00	0.010	1.41	0.01	1.41	0.0332	4.67
	High	362	2.04	0.060	2.94	0.030	1.47	0.000	0.00	0.01	0.49	0.0678	3.32
IG%	Low	364	10.08	0.380	3.77	0.090	0.89	0.000	0.00	0.03	0.30	0.392	3.89
	Normal	369	11.13	0.340	3.05	0.000	0.00	0.070	0.63	0.01	0.09	0.347	3.12
	High	362	12.13	0.350	2.89	0.090	0.74	0.000	0.00	0.05	0.41	0.365	3.01
IPF%	Low	364	19.34	0.810	4.19	0.000	0.00	0.000	0.00	0.11	0.57	0.817	4.23
	Normal	369	19.95	0.800	4.01	0.000	0.00	0.310	1.55	0.03	0.15	0.858	4.3
	High	362	19.99	0.730	3.65	0.450	2.25	0.000	0.00	0.1	0.50	0.863	4.32
RET-He (pg)	Low	364	25.01	0.150	0.60	0.080	0.32	0.270	1.08	0.34	1.36	0.466	1.86
	Normal	369	25.83	0.220	0.85	0.090	0.35	0.300	1.16	0.15	0.58	0.411	1.59
	High	362	27.64	0.370	1.34	0.150	0.54	0.340	1.23	0.39	1.41	0.654	2.36

Precision/Repeatability Study – Body Fluid Mode

Within-run precision studies were performed at three clinical sites using two high and two low residual body fluid samples for CSF, Pleural, Peritoneal and Synovial

fluid around medical decision levels and 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 ten consecutive times at three clinical sites. The mean, SD, and CV were calculated for each sample included in the study. The results of the Precision/Repeatability met the performance specifications (CV%) for the XN-Series analyzers.

Precision/Reproducibility – Body Fluid Mode

Precision/Reproducibility studies were performed on the XN-Series analyzers (XN-10, XN-20) Body Fluid Mode using two levels of quality control material (Low and High). Each level was run in duplicate twice each day for a minimum of 25 days using a single control lot at each of the three test sites. The results of the body fluid precision (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. All results met the acceptance criteria for both XN-10 and XN-20. Results of XN-10 are shown below.

Body Fluid Reproducibility (Combined Sites)

XN-10 Module													
Measurand	Control Level	N	Mean	Within-run		Between-run		Between-day		Between-site		Total	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
WBC-BF	Level 1	356	0.085	0.003	3.53	0.004	4.71	0.004	4.71	0.000	0.00	0.00640	7.53
	Level 2	356	0.288	0.009	3.13	0.010	3.47	0.011	3.82	0.010	3.47	0.02005	6.96
RBC-BF	Level 1	356	0.025	0.000	0.00	0.000	0.00	0.001	4.00	0.000	0.00	0.00100	4.00
	Level 2	356	0.073	0.001	1.37	0.000	0.00	0.002	2.74	0.000	0.00	0.00224	3.06
TC-BF	Level 1	356	0.085	0.003	3.53	0.004	4.71	0.004	4.71	0.000	0.00	0.00640	7.53
	Level 2	356	0.288	0.009	3.13	0.010	3.47	0.011	3.82	0.010	3.47	0.02005	6.96
MN#	Level 1	356	0.025	0.002	8.00	0.000	0.00	0.001	4.00	0.000	0.00	0.00224	8.94
	Level 2	356	0.087	0.006	6.90	0.001	1.15	0.003	3.45	0.000	0.00	0.00678	7.80
PMN#	Level 1	356	0.061	0.003	4.92	0.003	4.92	0.004	6.56	0.000	0.00	0.00583	9.56
	Level 2	356	0.200	0.009	4.50	0.009	4.50	0.011	5.50	0.010	5.00	0.01957	9.79
MN%	Level 1	356	29.32	2.33	7.95	1.05	3.58	1.68	5.73	1.82	6.21	3.56	12.14
	Level 2	356	30.62	2.08	6.79	0.84	2.74	1.69	5.52	1.96	6.40	3.42	11.19
PMN%	Level 1	356	70.79	2.33	3.29	1.05	1.48	1.68	2.37	1.64	2.32	3.47	4.90
	Level 2	356	69.38	2.08	3.00	0.84	1.21	1.69	2.44	1.96	2.83	3.42	4.94

c. Linearity:

Whole blood

Serial dilutions of known high concentration of K_2EDTA whole blood samples and control material which spanned the full measuring range of all direct measured parameters and related measurements were aspirated in the whole blood open cap manual mode at three clinical sites. Each serial dilution was run in duplicate. The method has been demonstrated to be linear from lower limit to upper limit and within measured allowable max % diff for each interval. Results of XN-10 are shown below. XN-20 has comparable performance.

Whole Blood Linearity – XN-10 Module

Parameter	Units	r^2	Slope	Intercept	Mean Replicate %Diff	Max Allowable %Diff	Range
SITE 1							
WBC	$10^3/\mu L$	1.00	1.00	-0.09	0.97	±3%	0.05-480.60
RBC	$10^6/\mu L$	0.99	1.02	-0.02	0.90	±2%	0.02-10.28
HGB	g/dL	0.99	1.01	-0.07	-0.73	±2%	0.0-26.9
HCT	%	0.99	1.02	-0.26	0.54	±3%	0.0-76.1
PLT-I	$10^3/\mu L$	1.00	0.99	-1.28	0.71	±5%	0-5217
PLT-F	$10^3/\mu L$	1.00	0.99	-1.28	0.71	±5%	0-5217
RET	%	0.99	0.96	-0.00	0.20	±20%	0.0-25.0
SITE 2							
WBC	$10^3/\mu L$	1.00	0.99	0.001	1.3	±3%	0.15-482.49
RBC	$10^6/\mu L$	0.99	1.00	-0.03	1.0	±2%	0.10-8.63
HGB	g/dL	0.99	1.01	-0.06	0.4	±2%	0.1-26.7
HCT	%	0.99	0.97	0.48	0.5	±3%	0.1-73.9
PLT-I	$10^3/\mu L$	1.00	0.99	8.26	1.5	±5%	8-5314
PLT-F	$10^3/\mu L$	1.00	0.99	9.48	0.7	±5%	9-5314
RET	%	0.99	1.00	0.01	1.6	±20%	0.0-24.1
SITE 3							
WBC	$10^3/\mu L$	1.00	0.99	0.12	1.0	±3%	0.01-468.64
RBC	$10^6/\mu L$	0.99	0.99	0.06	1.3	±2%	0.02-10.28
HGB	g/dL	1.00	0.99	0.002	0.4	±2%	0.0-32.7
HCT	%	1.00	1.00	-0.05	-1.16	±3%	0.3-96.2
PLT-I	$10^3/\mu L$	1.00	0.99	-1.66	1.45	±5%	7-6883
PLT-F	$10^3/\mu L$	0.99	0.86	11.58	2.0	±5%	7-3291
RET	%	0.99	0.99	-0.015	0.76	±20%	0.0-25.0

Body fluid

Linearity studies were performed at three clinical sites using serial dilutions of known high concentrations of body fluid samples which spanned the full measuring range of the WBC-BF, RBC-BF and TC-BF. 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. For the measured analytes, WBC-BF, RBC-BF and TC-BF by XN-Series, the method has been demonstrated to be linear from lower limit to upper limit and within measured allowable max % diff for each interval. Shown below are results for XN-10. Similar results were obtained for XN-20.

Body Fluid Linearity – XN-10 Module

Fluid Type	Parameter	Units	r^2	Slope	Intercept	Pooled Replicate %Diff	Max Allowable %Diff	Range
CSF	SITE 1							
	WBC-BF	$10^3/\mu L$	0.99	1.00	-0.0043	1.54	±3%	0.002-15.486
	RBC-BF	$10^6/\mu L$	0.99	1.00	0.0008	1.94	±2%	0.001-6.268
	TC-BF	$10^3/\mu L$	1.00	0.99	-0.007	1.76	±2%	0.002-15.648
	SITE 2							
	WBC-BF	$10^3/\mu L$	0.99	0.99	0.0003	0.06	±3%	0.001-9.569
	RBC-BF	$10^6/\mu L$	0.99	0.99	0.0020	0.38	±2%	0.001-5.312
	TC-BF	$10^3/\mu L$	0.99	0.99	0.0003	0.31	±2%	0.001-9.571
	SITE 3							
	WBC-BF	$10^3/\mu L$	1.00	0.99	0.00	1.07	±3%	0.001-11.067
	RBC-BF	$10^6/\mu L$	1.00	1.00	-0.001	0.52	±2%	0.001-6.034

Fluid Type	Parameter	Units	r^2	Slope	Intercept	Pooled Replicate %Diff	Max Allowable %Diff	Range
	TC-BF	$10^3/\mu L$	1.00	0.99	0.00	1.06	±2%	0.001-11.069
Pleural Fluid	SITE 1							
	WBC-BF	$10^3/\mu L$	1.00	0.96	0.0028	1.20	±3%	0.001-10.577
	RBC-BF	$10^6/\mu L$	1.00	1.00	0.000	0.42	±2%	0.001-5.409
	TC-BF	$10^3/\mu L$	1.00	0.96	0.0028	1.11	±2%	0.001-10.722
	SITE 2							
	WBC-BF	$10^3/\mu L$	1.00	0.99	0.0026	0.52	±3%	0.001-12.316
	RBC-BF	$10^6/\mu L$	1.00	0.99	0.0007	0.76	±2%	0.001-6.403
	TC-BF	$10^3/\mu L$	0.99	0.96	0.0169	0.50	±2%	0.001-12.317
	SITE 3							
	WBC-BF	$10^3/\mu L$	1.00	0.99	-0.0016	1.32	±3%	0.001-17.703
	RBC-BF	$10^6/\mu L$	0.99	1.00	-0.0015	0.32	±2%	0.001-5.402
	TC-BF	$10^3/\mu L$	0.99	0.99	0.0067	1.38	±2%	0.001-17.704
Peritoneal Fluid	SITE 1							
	WBC-BF	$10^3/\mu L$	0.99	0.98	0.0031	1.20	±3%	0.001-10.915
	RBC-BF	$10^6/\mu L$	1.00	0.99	0.0008	0.53	±2%	0.001-5.873
	TC-BF	$10^3/\mu L$	0.99	0.95	0.0155	1.20	±2%	0.001-10.915
	SITE 2							
	WBC-BF	$10^3/\mu L$	0.99	1.00	0.0037	0.41	±3%	0.002-14.368
	RBC-BF	$10^6/\mu L$	0.99	0.99	0.0003	0.06	±2%	0.001-9.569
	TC-BF	$10^3/\mu L$	0.99	1.00	0.0041	0.48	±2%	0.002-16.367
	SITE 3							
	WBC-BF	$10^3/\mu L$	1.00	0.99	0.0000	0.74	±3%	0.001-11.772
	RBC-BF	$10^6/\mu L$	1.00	1.00	0.0000	0.35	±2%	0.001-6.071
	TC-BF	$10^3/\mu L$	1.00	0.99	0.0000	0.74	±2%	0.001-11.774
Synovial Fluid	SITE 1							
	WBC-BF	$10^3/\mu L$	1.00	1.00	-0.015	0.28	±3%	0.002-11.491
	RBC-BF	$10^6/\mu L$	1.00	1.00	-0.004	1.76	±2%	0.001-5.516
	TC-BF	$10^3/\mu L$	1.00	1.00	-0.002	0.31	±2%	0.002-11.494
	SITE 2							
	WBC-BF	$10^3/\mu L$	1.00	1.00	-0.0002	0.35	±3%	0.001-14.333
	RBC-BF	$10^6/\mu L$	1.00	0.99	0.0001	0.28	±2%	0.001-8.637
	TC-BF	$10^3/\mu L$	1.00	0.99	0.0001	0.87	±2%	0.001-14.370
	SITE 3							
	WBC-BF	$10^3/\mu L$	1.00	0.99	-0.0047	1.61	±3%	0.001-20.227
	RBC-BF	$10^6/\mu L$	1.00	1.00	-0.0009	0.94	±2%	0.002-5.004
	TC-BF	$10^3/\mu L$	1.00	0.99	-0.0053	1.60	±2%	0.002-20.284

d. Carryover:

Whole Blood: - Carryover was evaluated by assaying whole blood samples with high WBC, RBC, HGB, and PLT counts three consecutive times followed immediately by testing samples with low target values around medical decision levels consecutively 3 times. Carryover effect was calculated for each measurand and results were within specifications (≤1.0%) for WBC, RBC, HGB and PLT.

Body Fluids: - Carryover was evaluated by assaying residual body fluid samples with high WBC-BF and RBC-BF counts three consecutive times followed immediately by testing samples with low target values around medical decision levels consecutively 3 times. Carryover effect was calculated for each measurand and results were within specifications (≤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-20 analyzer. Six whole blood samples from each of three donors were spiked with Bilirubin C from Interference Check A Plus (Sysmex Corp). Samples were mixed and measured three times by the whole blood mode of the instrument. There was no significant Bilirubin C interference up to a concentration of 39.4 mg/dL for WBC, RBC, HGB, HCT, PLT-I, PLT-F, RET#/%, RET-He, IPF parameters. There was no significant Bilirubin C interference up to a concentration of 15.8 mg/dL for IRF parameter.

A study was conducted to determine at what level Bilirubin F interferes with the hematology results of the XN-20 analyzer. Six whole blood samples from each of three donors were spiked with Bilirubin F from Interference Check A Plus (Sysmex Corp). Samples were mixed and measured three times by the whole blood mode of the instrument. There was no significant Bilirubin F interference up to a concentration of 37.4 mg/dL for WBC, RBC, HGB, HCT, PLT-I, PLT-F, RET#/%, IRF, RET-He parameters. There was no significant Bilirubin C interference up to a concentration of 29.9 mg/dL for IPF parameter.

A study was conducted to determine at what level Hemolytic Hemoglobin interferes with the hematology results of the XN-20 analyzer. Six whole blood samples from each of three donors were spiked with Hemolytic Hemoglobin from Interference Check A Plus (Sysmex Corp). Samples were mixed and measured three times by the whole blood mode of the instrument. There was no significant Hemolysis interference up to a concentration of 996 mg/dL for WBC, RBC, HCT, PLT-I, PLT-F, RET#/%, IRF, RET-He, IPF parameters. There was no significant Hemolysis interference up to a concentration of 199 mg/dL for HGB parameter.

A study was conducted to determine what level of Lipid interferes with the hematology results of the XN-20 analyzer. Six whole blood samples from each of three donors were spiked with Intralipid (Fresenius-kabi AB). Samples were mixed and measured three times by the whole blood mode of the instrument. There was no significant Intralipid interference up to a concentration of 55.98 OD for RBC, HCT, PLT-I, PLT-F, RET#/%, RET-He, IPF parameters. There was no significant Intralipid interference up to a concentration of 30.32 OD for WBC, IRF parameters and up to a concentration of 1.08 OD for HGB parameter.

A study was conducted to determine the level of Chyle which interferes with the hematology results of the XN-20 analyzer. Six whole blood samples from each of three donors were spiked with Chyle from Interference Check A Plus (Sysmex Corp). Samples were mixed and measured three times by the whole blood mode of the instrument. There was no significant Chyle interference up to a concentration of 2880 FTU for WBC, RBC, HCT, PLT-I, RET#/%, IRF, RET-He, IPF parameters. There was no significant Chyle interference up to a concentration of 2304 FTU for HGB parameter and up to a concentration of 576 FTU for PLT-F parameter.

f. *Background Counts:*

The XN-Series Analyzers (XN-10, XN-20) background specifications are as follows:

Whole Blood

Measurand	Background Limits
WBC	0.10 x 10^3/µL or less
RBC	0.02 x 10^6/µL or less
HGB	0.10 g/dL or less
PLT (RBC/PLT channel)	10 x 10^3/µL or less
PLT (PLT-F channel)	3 x 10^3/µL or less

Body Fluid

Measurand	Background Limits
WBC-BF	0.001 x 10^3/µL or less
RBC-BF	0.003 x 10^6/µL or less

2. Other Supportive Instrument Performance Data Not Covered Above:

a. Specimen Stability Studies:

Whole blood stability - Room temperature vs Refrigerated temperature
Thirty (30) normal residual K_2EDTA whole blood samples were evaluated at three clinical sites. Two sets of samples were collected from each donor (room temperature (RT) and refrigerated (LT)). The samples were run in duplicate on the XN-Series analyzers in the Automated Whole Blood Mode. 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 72 hours at RT (20-25ºC) and LT (2-8ºC). The mean, SD, CI and mean difference and/or percent difference were recorded for each sample. The stability for the XN-Series met the manufacturer's specifications for 24 hours at RT and 48 hours at LT.

Twelve (12) abnormal residual K_2EDTA whole blood samples were also evaluated by one clinical site. The residual samples were split into two sets of samples for each donor (RT and LT). The samples were run in singlet (due to limited sample volumes) on the XN-20 module in the Automated Whole Blood Mode. Each sample was tested at baseline or zero (0) time, 24 hours, 48 hours and 72 hours at RT (20-25ºC) and LT (2-8ºC). The mean, SD, CI and mean difference and/or percent difference were recorded for each sample. The results of the stability study using abnormal whole blood samples on the XN-20 module met the manufacturer's specifications for 24 hours at RT and 48 hours at LT.

Body fluid short term stability
Two different residual CSF, Pleural, and Peritoneal and Synovial fluids were evaluated at two test sites. Pleural, Peritoneal and Synovial fluids were collected in K_2EDTA anticoagulant and run in duplicate in the Body Fluid Mode. Each sample was carefully mixed by gentle hand inversion at least 10 times before analyzing on the XN-Series analyzers (XN-10 and XN-20) and tested at baseline (zero (0) time), 1 hour, 4 hours and 6 hours at room temperature (20-25ºC). Body

fluid samples should be analyzed within 1 hour of collection as demonstrated in the short term stability study.

b. Anticoagulant Comparison Study – K_2EDTA vs. K_3EDTA whole blood:
Anticoagulant comparison studies were performed to demonstrate comparability between K_2EDTA vs. K_3EDTA whole blood samples using the XN-Series analyzers (XN-10 and XN-20). A total of 46 paired whole blood samples (K_2EDTA vs. K_3EDTA) drawn from healthy Sysmex employees were used for this study. The samples were run in singlet on the XN-Series (XN-10, XN-20) and the results of the K_2EDTA sample results were compared to the corresponding results of the K_3EDTA sample for the same donor. Testing was performed in the Whole Blood Automated Sampler Analysis Mode. Of the 46 normal whole blood samples tested, 4 samples contained NRBCs (range 0.0-0.02 cells/μL) which is an insufficient number for linear correlation analysis. 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.

c. Comparison of venous whole blood samples to capillary whole blood:
Studies were performed to demonstrate comparability between K_2EDTA venous whole blood samples to K_2EDTA capillary whole blood samples using the XN-Series analyzers (XN-10 and XN-20). A total of 20 paired whole blood venous samples and capillary samples drawn from healthy Sysmex employees were used for this study. The samples were run in singlet on the XN-Series (XN-10, XN-20) 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 normal whole blood samples tested, 4 samples contained NRBCs (range 0.0-0.02 cells/μL) which is an insufficient number for linear regression analysis. The results of the linear regression analysis and bias between venous whole blood samples and capillary whole blood samples on the XN-Series analyzers met the acceptance criteria for all applicable parameters.

d. Comparison of K_2EDTA tubes and micro-collection tubes:
A total of 47 residual K_2EDTA whole blood samples (less than 8 hours old) collected by venipuncture blood draw were used to determine the presence or absence of matrix effect between K_2EDTA tubes and micro-collection tubes on the XN-Series analyzers (XN-10, XN-20). A total of 13 of these samples were diluted with normal saline to create near zero cell counts for the WBC, RBC and PLT parameters. Sample distribution included clinical medical decision levels and to the extent possible of the analytical measuring range. K_2EDTA whole blood samples were first analyzed in singlet in the Manual Mode Normal Tube position. Within two hours of analysis in the normal tube position, the samples were transferred to micro-collection tubes (without additive) and analyzed in the Manual Mode Micro-collection tube position. Of the 47 samples tested in the study, 1 sample failed to result a RET-He value. The results of the linear regression analysis and bias between the K_2EDTA tube and micro-collection tubes

on the XN-Series analyzers met the acceptance criteria for all applicable parameters.

e. Bridging Study (Pre-dilute Mode normal tube position and Pre-dilute Mode micro-collection tube position):
A total of 20 K_2EDTA (4 mL tubes) whole blood samples drawn from healthy Sysmex employees were used to determine the equivalency between the Manual Whole Blood Mode Pre-dilute Normal Tube Position and the Manual Whole Blood Mode Pre-dilute Micro-collection tube position. Pre-dilute (1:7) samples were prepared for each of the 20 samples by dispensing 420 µL of the analyzer's diluent into plain top tubes (3 mL tubes) then adding 70 µL of whole blood and mixing 10 times by gentle inversion. The plain top 3 mL tubes were analyzed in singlet on both XN-Series analyzers (XN-10 and XN-20) within 1 hour of dilution preparation in the Manual Whole Blood 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 Manual Whole Blood Pre-dilute Mode Micro-collection tube position (Cap Off). The pre-dilute mode automatically multiplies sample results before results are displayed therefore no additional calculation is required in this mode. 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-Series analyzers met the acceptance criteria in the Pre-dilute Mode for all applicable parameters.

f. Bridging Study – Comparison of Low WBC Mode normal tube position and Low WBC Mode micro-collection tube position:
Twenty duplicate K_2EDTA anticoagulated whole blood samples drawn from healthy Sysmex employees were selected to determine the equivalency between the Low WBC Mode normal tube position and the Low WBC Mode micro-collection tube position. One sample from each set of duplicate samples was centrifuged, the plasma removed and used to dilute (10-30 µL whole blood added to 400 µL plasma) the other uncentrifuged sample to create low concentrations of WBC ($\leq 1.0 \times 10^3/\mu L$). Each sample was mixed by gentle hand inversion 10 times and run in singlet in the Low WBC Mode Normal Tube Position on the XN-Series analyzers (XN-10 and XN-20). The samples were then transferred to micro-collection tubes (without additive) and run in the Low WBC Mode Micro-collection Tube Position (Cap Off) on both XN-Series analyzers within 1 hour of analysis of the Normal Tube Position. Statistical analysis results are not available for basophils and immature granulocytes due to the low frequency of these cell types seen in the normal samples. Of the 20 samples tested, there were no basophils seen (range 0.00-0.00 cells/µL) and 4 samples with immature granulocytes (range 0.00-0.04 cells/µL). 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 with the exception of PLT-I and LYMPH%. The PLT-I (r=0.9404 on the XN-20) has a slightly lower r value; however, the difference between the two devices were within the acceptable %Bias Limits. The LYMPH% (r=0.8472 on the XN-10) had a lower r value; however, the difference between the two devices were within the acceptable

%Bias Limits and the WBC parameter in which the LYMPH% is derived met both the correlation coefficient and bias acceptance limits.

g. Determination of limit of blank, lower limits of detection and quantitation:
Limit of Blank (LoB) – Whole Blood and Body Fluid Mode
The LoB was obtained from 60 repeated measurements of a single blank diluent sample (CELLPACK DCL) analyzed in the sampling modes for whole blood and body fluid. The mean, SD and LoB were calculated for both XN-10 and XN-20 analyzers. The LoB on both the XN-10 and XN-20 analyzers for whole blood parameters WBC, RBC, HGB, HCT, PLT-F and PLT-I is zero (0) cells/µL. The LoB on both the XN-10 and XN-20 analyzers for body fluid parameters WBC-BF, TC-BF, MN#, PMN# and RBC-BF is zero (0) cells/µL.

Limit of Detection (LoD), Limit of Quantitation (LoQ) – Whole Blood Mode
The LoD was obtained from three test runs of 60 repeated measurements taken from one low concentration sample for each run. The known concentration for each target sample was determined using the XE-5000 predicate method. The mean, SD and LoD were calculated for both XN-10 and XN-20 analyzers. The LoD on the XN-10 for WBC is 0.019 x 10^3µ/L, RBC is 0.007 x 10^6µ/L, HGB is 0.064 g/dL, HCT is 0.083 %, PLT-F is 0.862 x 10^3µ/L and PLT-I is 1.566 x 10^3µ/L. The LoD on the XN-20 for WBC is 0.012 x 10^3µ/L, RBC is 0.008 x 10^6µ/L, HGB is 0.041 g/dL, HCT is 0.083 %, PLT-F is 0.828 x 10^3µ/L and PLT-I is 1.314 x 10^3µ/L.

The LoQ was obtained from three test runs of 40 repeated measurements taken from one low concentration sample for each run. The known concentration for each target sample was determined using the XE-5000 predicate method. The mean, SD and LoQ were calculated for both XN-10 and XN-20 analyzers. The LoQ and lower bound of the Analytical Measuring Range (AMR) on both the XN-10 and XN-20 analyzers for WBC is 0.03 x 10^3µ/L, RBC is 0.01 x 10^6µ/L, HGB is 0.1 g/dL, HCT is 0.1 %, PLT-F and PLT-I is 2 x 10^3µ/L.

Limit of Detection (LoD), Limit of Quantitation (LoQ) – Body Fluid Mode
The LoD was obtained from three test runs of 60 repeated measurements taken from one low concentration sample for each run. The known concentration for each target sample was determined using the XE-5000 predicate method. The mean, SD and LoD were calculated for both XN-10 and XN-20 analyzers. The LoD on both the XN-10 and XN-20 analyzers for WBC-BF, TC-BF, MN#, and PMN# is 0.002 x 10^3cells/µL and RBC-BF is 0.001 x 10^6cells/µL.

The LoQ was obtained from three test runs of 40 repeated measurements taken from one low concentration sample for each run. The known concentration for each target sample was determined using the XE-5000 predicate method. The mean, SD and LoQ were calculated for both XN-10 and XN-20 analyzers. The LoQ and lower bound of the Analytical Measuring Range (AMR) on both the XN-10 and XN-20 analyzers for WBC-BF, TC-BF, MN#, and PMN# is 0.003 x 10^3cells/µL and RBC-BF is 0.002 x 10^6cells/µL.

h. Reference Intervals:
Adult reference intervals (Normal Population Reference Ranges) were assessed for

the XN-Series analyzers by comparing K_2EDTA anticoagulated samples collected from healthy male (n=48) and female (n=56) 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 the results were outside the proposed reference interval providing verification of the previously established 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.