510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM

A. 510(k) Number:

K182389

B. Purpose for Submission:

Expand Intended Use to include pediatric subjects under the age of 2 years old.

C. Manufacturer and Instrument Name:

Sysmex America Inc., Sysmex® XN-L Automated Hematology Analyzer

D. Type of Test or Tests Performed:

The Sysmex XN-L Automated Hematology Analyzer (hereafter, the XN-L analyzer) classifies and enumerates 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, RET%/#, 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 (CSF), peritoneal, pleural and synovial fluids.

E. System Descriptions:

1. Device Description:
   The XN-L analyzer is a quantitative multi-parameter automated differential cell counter that classifies and enumerates whole blood and body fluid parameters by means of electrical impedance, laser light scattering, and fluorescent labeling. Cell counts and parameters are performed on whole blood samples collected in K_2EDTA or K_3EDTA anticoagulant, body fluids (peritoneal, pleural and synovial) collected in K_2EDTA anticoagulant and CSF collected without anticoagulant. The instrument consists of two principal units: (1) the Main Unit which will aspirate, dilute, mix, and analyze whole blood and body fluid samples and (2) the Pneumatic Unit which supplies pressure and vacuum to the analyzer.

   The XN-L analyzer has an external monitor with touch screen capability that is used to operate the instrument and process data from the Main Unit. The monitor also allows for operator interfacing with the instrument by use of a panel keyboard.

2. Principles of Operation:
   The XN-L analyzer analyzes samples using the following methods: DC Sheath Flow Detection method, Flow Cytometry method using a semiconductor laser, and SLS (cyanide-free sodium lauryl sulfate) hemoglobin method. Particle characterization and identification is based on detection of forward scatter, fluorescence, and adaptive cluster analysis. The XN-L analyzer automatically classifies cells from whole blood and body

fluids and carries out all processes automatically from aspiration of the sample to result output.

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. In the Sampler 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. The Sampler Mode is used for processing of whole blood samples. In the Manual 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. The samples in the Manual Mode can be analyzed with the cap on or off. The Manual Mode is used for processing whole blood and body fluid samples.

6. Calibration:
   The XN CAL calibrator (K160585) is used for calibration of the WBC, RBC, HGB, HCT, PLT and RET parameters. XN CAL is used for the calibration and calibration verification of Sysmex XN series (XN-10, XN-11, XN-20, XN-21, XN-L) analyzers. Calibration is performed as needed (e.g., when QC data is fluctuating) to ensure accuracy of the system.

7. Quality Control:
   The XN-L CHECK (K160586) is used as quality control (three levels) for Sysmex XN-L analyzers. XN-L CHECK™ is an in-vitro diagnostic product that contains the following: stabilized red blood cell component(s), stabilized white blood cell component(s), and stabilized platelet component(s) in a preservative medium.

   XN CHECK (K160590) is used as quality control (three levels) for Sysmex XN series (XN-10, XN-11, XN-20, XN-21, XN-L) analyzers. XN CHECK is an in-vitro diagnostic product that contains the following: stabilized red blood cell component(s), stabilized white blood cell component(s), stabilized platelet component(s), and stabilized nucleated red blood cell component(s) in a preservative medium.

XN CHECK BF (K160588) is used as quality control (two levels) for Sysmex XN series (XN-10, XN-11, XN-20, XN-21, XN-L) analyzers. Assayed parameters include: WBC-BF, RBC-BF, MN%, PMN%, TC-BF#.

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 Sysmex XN-L analyzer is a quantitative multi-parameter automated hematology analyzer intended for in vitro diagnostic use in screening patient populations found in clinical laboratories. The XN-L analyzer classifies and enumerates the following parameters in venous and capillary whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, IG%/#, RDW-CV, RDW-SD, MPV, RET%/#, 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, peritoneal, pleural, and synovial fluids. Whole blood should be collected in K2 or K3EDTA anticoagulant and peritoneal, pleural, 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 XN-Series (XN-10, XN-20) Automated Hematology Analyzer, K112605

2. Comparison with Predicate Device:

Similarities		
Item	Candidate Sysmex XN-L analyzer K182389	Predicate Sysmex XN-Series (XN-10)[a] K112605
Intended Use	The Sysmex XN-L analyzer is a quantitative multi-parameter automated hematology analyzer intended for in vitro diagnostic use in screening patient populations found in clinical laboratories. The XN-L analyzer classifies and enumerates the following parameters in venous and capillary whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, IG%/#, RDW-CV, RDW-SD, MPV, RET%/#, 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, 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. The use of anticoagulants with CSF specimens is neither required nor recommended.	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 WBCBF, 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.
Specimen Type	Whole Blood and Body Fluids (CSF and peritoneal, pleural, synovial fluids)	Same
Test Principle	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%/#,	Same

Similarities		
Item	Candidate Sysmex XN-L analyzer K182389	Predicate Sysmex XN-Series (XN-10)[a] K112605
	EO%/#, BASO%/#, RDW-CV, RDW-SD, MPV, RET%/#, IRF, IG%/#, RET-He# Body Fluid Mode: WBC-BF, RBC-BF, MN%/#, PMN%/#,TC-BF#	
Reagents	CELLPACK DCL (Diluent) CELLPACK DFL (Diluent) Lysercell WDF (Lyse) Fluorocell WDF (Stain) Fluorocell RET (Stain) SULFOLYSER (Lyse)	Same
Analysis Modes	Sampler Analysis Mode (rack autoloader) Whole Blood Mode Manual Analysis Mode Whole Blood Mode; LWBC Analysis Mode; Pre-Dilute Analysis Mode; Body Fluid Mode	Same
Sample Aspiration/ Fluidic Pathway	Single Pathway	Same
Measuring Channels	RBC/PLT, HGB, RET, WDF	Same
Controls/Calibrators/ Linearity Material	Whole Blood XN CHECK 3 Levels (K160590); XN CAL (K160585); Body Fluid XN CHECK BF 2 Levels (K160588) Whole Blood Linearity Range Check X III (K960557); Retic Chex (K000115)	Same
Cleaning Detergent	CELLCLEAN AUTO	Same
Software/ Hardware	Rule based rerun/reflex	Same

Differences		
Item	Candidate Sysmex XN-L analyzer K182389	Predicate Sysmex XN-Series (XN-10)[a] K112605
Parameters	Not Available	PLT (PLT-F), NRBC%/#, IPF
Reagents	Not Available	K112605 Lysercell WNR (Lyse) Fluorocell WNR (Stain) Fluorocell PLT (Stain)
Measuring Channels	Not Available	WNR, PLT-F
Controls/Calibrators	Not Available XN-L CHECK[b]	XN CAL PF – (K120747) Not Available
Throughput	Whole Blood Mode 60 samples/hour maximum depending on mode used. Body Fluid Mode 30 samples/hour maximum	Whole Blood Mode 100 samples/hour maximum depending on mode used. Body Fluid Mode 40 samples/hour maximum
Sample Aspiration Volumes	Sampler Mode - 25 µL Manual (Closed Cap) Mode - 25 µL Manual (Open Cap) Mode - 25 µL Dilution Mode - 70 µL Body Fluid Mode - 70 µL	Sampler Mode - 88 µL Manual (Closed Cap) Mode - 88 µL Manual (Open Cap) Mode - 88 µL Dilution Mode - 70 µL Body Fluid Mode - 88 µL

[a] Intended use for the predicate analyzer was cleared in submission K112605. All information listed for the predicate analyzer refers to the XN-10 module.
[b] Control material specific for the XN-L analyzer.

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

- CLSI C28-A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition
- CLSI EP06-A Evaluation of the Linearity of Quantitative Measurement Procedures: Statistical Approach; Approved Guideline
- CLSI EP12-A2, User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline - Second Edition
- CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI H20-A2 Reference Leukocyte (WBC) Differential Count (Proportional) And Evaluation Of Instrumental Methods; Approved Standard-Second Edition
- CLSI H26-A2, Validation, Verification, and Quality Assurance of Automated Hematology Analyzer; Approved Guideline - Second Edition
- IEC 60825-1:2007 Safety of laser products – Part 1: Equipment classification and requirements
- IEC 61010-1:2001 Safety requirements for electrical equipment for measurement, control

and laboratory use – Part 1: General requirements

- IEC 61010-2-081:2001+A1 Safety requirements for electrical equipment for measurement, control and laboratory use – Part 2-081: Particular requirements for automatic and semi-automatic laboratory equipment for analysis and other purposes
- IEC 61010-2-101:2002 Safety requirements for electrical equipment for measurement, control and laboratory use – Part 2-101: Particular requirements for *in vitro* diagnostic (IVD) medical equipment
- IEC 61326-2-6:2005 Electrical equipment for measurement, control and laboratory use – EMC requirements – Part 2-6: Particular requirements – *In vitro* diagnostic (IVD) medical equipment

J. Performance Characteristics:

1. Analytical Performance:

a. Method comparison:

i. Method comparison - > 2 years of age:
Refer to K160538

ii. Method comparison - ≤ 2 years of age:

Whole Blood Studies (excluding reticulocyte parameters - RET, IRF, Ret-He):
A total of 52 pediatric samples under the age of 2 years old were collected across three clinical pediatric sites. The residual specimens were collected in K_2EDTA according to the manufacturer's recommendations. All samples were tested within 8 hours of collection. Samples were analyzed on both the XN-10 analyzer and the XN-L in singlet by the labeled procedures within 2 hours of each other.

Deming regression analyses were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals (CI) and correlation coefficient). The 95% CI and estimates of the bias/difference were determined for each parameter. All results were within the pre-defined acceptance criteria.

All sites combined:

Parameter (unit)	Result Range	Correlation Coefficient	Slope (95% CI)	Intercept (95% CI)
WBC ($10^3/\mu L$)	2.64 – 23.85	0.9982	0.925 (0.909, 0.941)	0.199 (0.017, 0.380)
RBC ($10^6/\mu L$)	2.74 – 5.78	0.994	1.015 (0.984, 1.047)	-0.064 (-0.200, 0.071)
HGB (g/dL)	7.1 – 15.9	0.9981	1.032 (1.014, 1.050)	-0.11 (-0.32, 0.10)
HCT	22.0 – 45.8	0.9833	0.975	0.92

Parameter (unit)	Result Range	Correlation Coefficient	Slope (95% CI)	Intercept (95% CI)
(%)			(0.925, 1.026)	(-0.88, 2.73)
MCV (fL)	72.8 – 103.1	0.922	1.041 (0.924, 1.157)	-3.2 (-12.91, 6.50)
MCH (pg)	23.6 – 33.0	0.968	1.003 (0.931, 1.075)	0.53 (-1.41, 2.47)
MCHC (g/dL)	29.5 – 34.7	0.7726	0.878 (0.707, 1.049)	4.6 (-0.93, 10.13)
PLT ($10^3/\mu L$)	135 – 888	0.9924	1.119 (1.080, 1.158)	-19.6 (-35.4, -3.8)
RDW-SD (fL)	34.5 – 58.2	0.956	0.992 (0.909, 1.076)	1.57 (-1.88, 5.02)
RDW-CV (%)	11.7 – 17.4	0.983	0.996 (0.944, 1.048)	0.29 (-0.42, 1.00)
MPV (fL)	8.1 – 12.5	0.934	1.019 (0.914, 1.124)	0.1 (-0.94, 1.14)
NEUT# ($10^3/\mu L$)	0.04 – 19.46	0.9992	0.93 (0.920, 0.941)	0.036 (-0.027, 0.099)
LYMPH# ($10^3/\mu L$)	0.79 – 12.93	0.9966	0.93 (0.908, 0.952)	0.039 (-0.079, 0.156)
MONO# ($10^3/\mu L$)	0.21 – 3.16	0.9729	0.933 (0.871, 0.995)	0.05 (-0.017, 0.117)
EO# ($10^3/\mu L$)	0.00 – 2.24	0.9977	0.88 (0.863, 0.897)	0.007 (0.000, 0.013)
BASO# ($10^3/\mu L$)	0.00 – 0.16	0.6237	1.348 (1.031, 1.664)	0.011 (-0.004, 0.026)
IG# ($10^3/\mu L$)	0.00 – 0.20	0.8999	0.738 (0.643, 0.834)	-0.002 (-0.008, 0.003)
NEUT% (%)	0.7 – 81.5	0.9994	0.996 (0.986, 1.006)	-0.05 (-0.51, 0.41)
LYMPH% (%)	10.9 – 87.8	0.9973	0.977 (0.957, 0.997)	0.65 (-0.43, 1.72)
MONO% (%)	4.1 – 17.4	0.9236	1.013 (0.900, 1.125)	0.31 (-0.78, 1.41)
EO% (%)	0.0 – 11.6	0.9959	0.964 (0.939, 0.988)	0.01 (-0.06, 0.08)
BASO% (%)	0.0 – 1.2	0.3733	2.258 (1.643, 2.873)	-0.15 (-0.42, 0.12)
IG % (%)	0.0 – 1.2	0.8464	1.011 (0.852, 1.171)	-0.09 (-0.16, -0.03)

Reticulocyte parameters (RET, IRF, Ret-He):

A total of 37 pediatric samples (1 month – 2.7 years) for the reticulocyte parameters were collected at one clinical site. The residual de-identified specimens were collected in K_2EDTA following manufacturer's recommendations. All samples

were tested within 8 hours of collection. Samples were analyzed on both the XN-10 analyzer and the XN-L in singlet by the labeled procedures within 2 hours of each other.

Deming regression analyses were used to estimate the parameters of the regression model (slope, intercept, 95% confidence intervals (CI) and correlation coefficient). The 95% CI and estimates of the bias/difference were determined for each parameter. All results were within the pre-defined acceptance criteria.

All sites combined:

Parameter	Result Range	Correlation Coefficient	Slope (95% CI)	Intercept (95% CI)
RET ($10^3/\mu L$)	0.0040 – 0.2154	0.9062	0.977 (0.831, 1.122)	-0.009 (-0.01994, 0.00126)
RET (%)	0.16 – 6.45	0.9060	0.946 (0.805, 1.087)	-0.206 (- 0.487, 0.076)
IRF (%)	1.5 – 42.9	0.9041	0.971 (0.824, 1.117)	-0.200 (-2.78, 2.38)
RET-He (pg)	22.6 – 35.5	0.9552	1.045 (0.938, 1.152)	-4.100 (-7.26, -0.94)

b. Precision/Reproducibility:
Refer to K160538

c. Linearity:
Refer to K160538

d. Carryover:
Refer to K160538

e. Interfering Substances:
Refer to K160538

2. Other Supportive Instrument Performance Data Not Covered Above:

a. Sample Stability
Refer to K160538

b. Verification of Reference Intervals

i. *Body Fluids*
Refer to K160538

ii. *Reference range - pediatrics > 2 years old:*
Refer to K160538

iii. Reference range - pediatric birth to ≤ 2 years

Two peer-reviewed references were cited to substantiate the reference intervals for pediatrics.

Reference Ranges for WBC, RBC, HGB, HCT, MCV, MCH, PLT, RDW-SD, RDW-CV, MPV, NEUT#, NEUT%, LYMPH#, LMPH%, MONO#, MONO%, EO#, EO%, BASO%, RET#, RET%, IRF%, IG#:
Soldin, S.J., Brugnara, C., and Wong, E.C. 2005. Pediatric Reference Intervals, Fifth Edition, AACC Press, Washington, DC.

Reference Ranges for BASO#, IG #, IG%, MCHC:
Soldin, S. J.,Brugnara, C., and Wong, E.C. 2007. Pediatric Reference Intervals, Sixth Edition, AACC Press, Washington, DC.*c. Matrix Studies*

Measurand	Units	Females	Males	Combined[1] RI Male/Females
WBC	x 10^3/µL	5.9 – 15.8	6.5 – 16.7	5.9 – 16.7
RBC	x 10^6/µL	3.55 – 4.83	3.24 – 5.08	3.24 – 5.08
HGB	g/dL	10.7 – 16.4	10.2 – 16.6	10.2 – 16.6
HCT	%	30.5 – 47.7	29.1 – 47.4	29.1 – 47.7
MCV	fL	76.6 – 105.4	75.6 – 106.3	75.6 – 106.3
MCH	pg	26.5 – 36.3	26.0 – 36.4	26.0 – 36.4
MCHC	g/dL	33.7 – 35.7	33.6 – 35.7	33.6 – 35.7
PLT	x 10^3/µL	95.0 – 430	120 – 471	95.0 – 471
RDW-SD	fL	34.9 – 65.7	35.3 – 61.7	34.9 – 65.7
RDW-CV	%	13.3 – 17.8	13.5 – 18.2	13.3 – 18.2
MPV	fL	7.3 – 9.9	7.3 – 9.3	7.3 – 9.9
NEUT	x 10^3/µL	2.2 – 11.4	2.2 – 9.4	2.2 – 11.4
NEUT	%	15.7 – 69.3	14.6 – 69.2	14.6 – 69.3
LYMPH	x 10^3/µL	1.2 – 5.7	1.4 – 5.6	1.2 – 5.7
LYMPH	%	8.0 – 70.0	9.0 – 68.0	8.0 – 70.0
MONO	x 10^3/µL	0.1 – 5.0	0.2 – 3.5	0.1 – 5.0
MONO	%	4.0 – 19.0	4.0 – 18.0	4.0 – 19.0
EO	x 10^3/µL	0.0 – 0.4	0.0 – 0.5	0.0 – 0.5
EO	%	1.0 – 6.0	1.0 – 7.0	1.0 – 7.0
BASO	x 10^3/µL	0.0 – 0.1	0.0 – 0.1	0.0 – 0.1
BASO	%	0.0 – 1.0	0.0 – 1.0	0.0 – 1.0
RET	%	0.4 – 3.7	0.4 – 4.8	0.4 – 4.8
RET	x 10^3/µL	35.0 – 120.0	29.0 – 104.0	29.0 – 120.0
RET-He[2]	pg	23.9 – 30.9	22.5 – 31.8	22.5 – 31.8
IRF	%	11.4 – 35.1	11.4 – 35.1	11.4 – 35.1
IG	%	0.0 – 1.7	0.0 – 1.7	0.0 – 1.7
IG	x 10^3/µL	0.00 – 0.28	0.00 – 0.28	0.0 – 0.28

[1] Combined Reference Intervals (RI) - The lowest and highest value of the above female and male ranges were used to define the lower and upper range for the combined RI for pediatric subgroup birth to <2 years listed in the above table.

d. Bridging Studies
Refer to K160538

e. Determination of limit of Blank, lower limits of detection and quantitation:
Refer to K160538

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.