510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K160585

B. Purpose for Submission:

To expand the intended use of an existing cleared calibrator (XN CAL; K141962) for use on an additional analyzer, the Sysmex XN-L Analyzer. The XN CAL has previously been cleared for use on other Sysmex XN Series analyzers – the XN-10, XN-11, XN-20, and XN-21 analyzers.

C. Measurand:

Assayed hematology parameters: WBC (10^3/μL), RBC (10^6/μL), HGB (g/dL), HCT (%), PLT (10^3/μL), and RET (%)

D. Type of Test:

Quantitative

E. Applicant:

Streck, Inc.

F. Proprietary and Established Names:

XN CAL

G. Regulatory Information:

1. Regulation section:

   21 CFR § 864.8150, Calibrator for cell indices

2. Classification:

   Class II

3. Product code:

   KRX, Calibrator for cell indices

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use(s):

   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. Assayed parameters include: WBC (10^3/µL), RBC (10^6/µL), HGB (g/dL), HCT (%), PLT (10^3/µL), and RET (%).

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Sysmex XN series (XN-10, XN-11, XN-20, XN-21, XN-L) analyzers

I. Device Description:

XN CAL 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. The product is packaged in polypropylene plastic vials with screw caps. The vials will be packaged in five-welled or one-welled vacuum formed clamshell container with the Instructions for Use (IFU) assay sheet. The product must be stored at 2 – 8°C.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   XN CAL

2. Predicate 510(k) number(s):

   K141962

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	XN CAL is used for the calibration and calibration verification of Sysmex XN series hematology analyzers. Assayed parameters include: WBC (10^3/µL), RBC (10^6/µL), HGB (g/dL), HCT (%), PLT (10^3/µL), and RET (%).	Same
Reagents	XN CAL 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.	Same
Storage Conditions	2–8°C	Same
Open Vial Stability	4 hours	Same

Differences		
Item	Device	Predicate
Intended Use	XN CAL is used for the calibration and calibration verification of the following Sysmex XN series hematology analyzers: XN-10, XN-11, XN-20, XN-21, and XN-L.	XN CAL predicate is NOT cleared for calibration and calibration verification of XN-L analyzers.
Closed Vial Stability	35 days	49 days

K. Standard/Guidance Document Referenced (if applicable):

CLSI H7-A3: Procedure of Determining Packed Cell Volume by the Microhematocrit Method; Approved Standard – Third Edition.

CLSI H15-A3: Reference and Selected Procedures for the Quantitative Determination of Hemoglobin in Blood; Approved Standard – Third Edition.

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

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.

L. Test Principle:

XN CAL was designed to function as a substitute for fresh whole blood to calibrate the Sysmex XN10/20, XN 11/21, and XN-L series hematology analyzers. This product is for *in-vitro* diagnostic use to calibrate the following parameters: RBC (10^6/µL), HGB (g/dL), HCT (%), PLT (10^3/µL), WBC (10^3/µL), and RET (%).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

i. *Multi-site reproducibility study:* Data was collected from Sysmex XN-L model analyzers at three sites – Streck, Sysmex-Buffalo Grove, and Sysmex-Mundelein with three different operators. Three separately manufactured lots of XN CAL were tested on each analyzer. The study was conducted over the course of 5 days, with three runs per day, and two replicates per run (5 days x 3 runs x 2 replicates x 3 lots x 3 sites). The means for each of the assayed parameters for each lot are indicated in Table 1, below. The total reproducibility estimates (Table 2, below) for each parameter for each lot include the repeatability (within-run), between-run, between-day, and between-site precision estimates. Results across the three separately manufactured lots of XN CAL demonstrated consistent recovery across multiple instruments, at multiple sites.

Table 1: Performance of XN CAL On Three XN-L Analyzers (3 sites) – Mean Values

		Parameter Mean					
Lot	**N**	**WBC**	**RBC**	**HGB**	**HCT**	**PLT**	**RET**
Lot 6144*	90	7.26	4.36	12.9	36.7	243	2.23
Lot 6172*	90	7.23	4.36	12.3	34.9	246	2.26
Lot 6200*	90	7.32	4.40	12.5	35.4	245	2.20

* = Within lot

Table 2: Performance of XN CAL On Three XN-L Analyzers (3 sites) – Variability Estimates

	Reproducibility Estimates for Each Parameter											
Lot	**WBC**		**RBC**		**HGB**		**HCT**		**PLT**		**RET**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Lot 6144*	0.16	2.2	0.06	1.3	0.1	1.1	0.9	2.3	8	3.1	0.13	5.9
Lot 6172*	0.21	2.9	0.05	1.2	0.1	1.2	0.7	2.1	10	4.1	0.17	7.4
Lot 6200*	0.18	2.4	0.05	1.2	0.1	1.1	0.8	2.3	12	4.7	0.15	7.0

* = Within lot

ii. *Internal precision study:* Performance data provided by the closed-vial stability study was used to support the internal precision study. In this study, performance of three (3) lots of XN CAL was evaluated at one site, on one instrument, for 21 non-consecutive days, two vials per day, and two replicates per vial. The internal precision for each lot of XN CAL was consistent across lots for each assayed parameter (see Tables 3 and 4, below). Total variability estimates (within-lab precision) included repeatability (within-run), between-vial, and between-day (Table 4, below).

Table 3: XN CAL Internal Precision Study – Mean Values

		Parameter Mean					
Lot	**N**	**WBC**	**RBC**	**HGB**	**HCT**	**PLT**	**RET**
Lot 5201*	80	7.28	4.40	11.7	34.5	237	2.48
Lot 5229*	80	7.18	4.44	12.0	35.4	236	2.31
Lot 5257*	80	7.33	4.38	12.1	35.4	232	2.27

* = Within lot

Table 4: Within Lab Precision for XN CAL

	Total variability (within-lab precision) for Each Parameter											
Lot	**WBC**		**RBC**		**HGB**		**HCT**		**PLT**		**RET**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Lot 5201*	0.12	1.7	0.03	0.6	0.1	0.6	0.3	0.8	4	1.9	0.08	3.3
Lot 5229*	0.11	1.6	0.03	0.8	0.1	0.6	0.4	1.0	5	2.3	0.07	3.2
Lot 5257*	0.12	1.6	0.03	0.8	0.1	0.6	0.3	0.7	5	2.0	0.07	3.3
Between Lots	0.08	1.1	0.03	0.8	0.2	1.8	0.5	1.5	3	1.2	0.11	4.7

* = Within lot

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Value Assignment:

Value assignment for the three lots of XN CAL evaluated in this submission was based on data collected across three XN-L instruments at three sites. Data was collected across three separately manufactured lots over the course of 5 non-consecutive days, with three (3) runs per day, and two (2) replicates per run. All assay ranges assigned to each lot for each of the parameters are based on the total reproducibility estimated from the multi-site reproducibility study. Assay values were assigned to the following parameters: RBC (10^6/µL), HGB (g/dL), HCT (%), PLT (10^3/µL), WBC (10^3/µL), and RET (%). Future lots of XN CAL will be value assigned at one site by a minimum of one operator. Five repeat measurements will be taken from two separate vials of calibrator and assayed in a single run on each of the 2 days. The average of the 20 individual measurements will be used for value assignment. All lot specific assay values will be included on the lot specific assay

sheet for each manufactured lot of control. This assay sheet will be included in each product package. Instruments at Streck are whole blood calibrated as per CLSI H26-A2 and the individual parameters are traceable to reference methods found in CLSI H7-A3, CLSI H15-A3, and ICSH Expert Panel on Cytometry publications (Clin. Lab. Haemat. 1998. v10, 203-212; and Am. J. Clin. Pathol. 2001. v115, 460-464).

Traceability:

The instruments maintained at Streck and used for value assignment for XN CAL measurands were calibrated with whole blood in accordance with CLSI H26-A2 "*Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard – Second Edition*," and are traceable to the following reference methods:

- WBC and RBC: Reference method for the enumeration of erythrocytes and leucocytes, ICSH Expert Panel on Cytometry, Clin Lab Haematol. 1994; 16, 131-138. Counts are performed on SCC (Semi-automated Single Channel counter), a volumetric manometer semi-automated electronic impedance cell counter.
- HGB: Recommendation for reference method for haemoglobinometry in human blood (ICSH standard 1995) and specification for international haemiglobincyanide standard (4th edition), ICSH Expert Panel on Haemoglobinometry, J Clin Pathol 1996; 49: 271-274.
- HCT: Recommendations for Reference Method for the Packed Cell Volume (ICSH Standard 2001), ICSH Expert Panel on Cytometry, Clin Lab Hematol. 2001; 7:148-170.
- PLT: Platelet count values are determined by using a Neubauer Improved hemacytometer counting chamber and the bioanalytic® GmbH Thrombo-tic® PLT counting kit. This method is based on the procedure developed by Brecher and Cronkite.
- RET%: Methods for Reticulocyte Counting (Automated Blood Cell Counters, Flow Cytometry, and Supravital Dyes); Approved Guideline – Second Edition Manual method CLSI H44-A2.
- CLSI Document H15-A3, Reference and Selected Procedures for the Quantitative Determination of Hemoglobin in Blood, December, 2000.

Reagent Stability:

i. *Open-vial stability*: A 4-hour real-time open-vial stability study was conducted at one site on the XN-L model analyzer. Throughout the collection of the open-vial stability data, the calibrator was stored as indicated in the instructions for use. Each vial was stored at 2–8°C and removed for testing. After testing, the vial was returned to 2–8°C until the next testing event. One vial of calibrator from each of the three lots was analyzed in four replicates on one day over a period of 5 hours (times 0, 2, 4, and 5 hours; n=16 measurements), on one analyzer. Stability performance of each lot of calibrator was assessed in terms of

parameter drift over time (for each parameter), as described in CLSI EP25-A – "*Evaluation of Stability of In Vitro Diagnostic Agents; Approved Guideline*." Values associated with each parameter, for each lot, and at each time point were within the acceptable value range, supportive of a 4-hour open vial stability claim.

ii. *Closed-vial stability*: A real-time, 35-day closed-vial study was conducted internally on one Sysmex XN-L model analyzer by one operator. Two vials of calibrators from each of the three lots were analyzed in duplicate over the course of 38–39 days (with data collected every 4 days), providing measurements for 21 non-consecutive days. Stability performance of each lot of calibrator was assessed in terms of parameter drift over time (for each parameter), as described in CLSI EP25-A – "*Evaluation of Stability of In Vitro Diagnostic Agents; Approved Guideline*." Values associated with each parameter, for each lot, and at each time point were within the acceptable value range, supportive of a 35-day closed-vial stability claim.

d. Detection limit:

Not applicable

e. Analytical specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. *Other clinical supportive data (when a. and b. are not applicable)*:

Not applicable

4. Clinical cut-off**:**

Not applicable

5. Expected values/Reference range:

All lot specific assay values will be included on the lot specific assay sheet for each manufactured lot of calibrators. This assay sheet will be included in each product package.

N. Proposed Labeling:

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

O. Conclusion:

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