

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k100790

B. Purpose for Submission:

Modification of the LIN-X Linearity Control – will offer seven vials (Levels 1 – 7) with addition of WBC parameter to Level 6.

C. Measurand:

WBC, RBC, HGB, PLT

D. Type of Test:

Quantitative

E. Applicant:

Beckman Coulter, Inc.

F. Proprietary and Established Names:

COULTER® LIN-X Linearity Control

G. Regulatory Information:

1. Regulation section:

21 CFR 864.8625, Hematology quality control mixture

2. Classification:

Class II

3. Product code:

JPK, Mixture, Hematology quality control

4. Panel:

81 (Hematology)

H. Intended Use:

1. Intended use(s):

COULTER® LIN-X Linearity Controls are intended to assess calibration and verify the reportable range of Coulter® Cellular Analysis Systems listed in the TABLE OF EXPECTED RESULTS in conjunction with specific COULTER reagents. Refer to Instructions for Use

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

Not applicable.

4. Special instrument requirements:

For use on DxH™ 300 the DxH™ 300C Analyzers

I. Device Description:

COULTER® LIN-X Linearity Control is a reference product prepared from treated, stabilized human erythrocytes in an isotonic medium. LIN-X Linearity Control also contains a stabilized, platelet-sized component, and fixed erythrocytes to simulate leukocytes. The WBC, RBC, HGB and PLT concentrations span the instrument's reportable range. Results from repeated measurements for each concentration are compared to the established expected range to assess the instrument's calibration and verify the reportable range.

J. Substantial Equivalence Information:

1. Predicate device name(s):
COULTER® LIN-X Linearity Control
2. Predicate K number(s):
k081641
3. Comparison with predicate:

Similarities		
<i>Item</i>	<i>COULTER® LIN-X Linearity Control k100790 (7 Levels)</i>	<i>COULTER® LIN-X Linearity Control k081641 (12 Levels)</i>
Intended use	COULTER® LIN-X Linearity Controls are intended to assess calibration and verify the reportable range of Coulter® Cellular Analysis Systems listed in the TABLE OF EXPECTED RESULTS in conjunction with specific COULTER reagents. Refer to Instructions for Use.	Same.
Product Description	COULTER® LIN-X Linearity Controls are stabilized human blood components whose WBC, RBC, HGB and PLT concentrations span the instrument's reportable range. Results from repeated measurements for each concentration are compared to the established expected range to assess the instrument's calibration and verify the reportable range.	Same
Assay Parameters	WBC, RBC, HGB, and PLT Level 6 also assayed for WBC	WBC, RBC, HGB, and PLT, WBC not included in Level 6
Manufacturing Process	LIN-X linearity controls are prepared from pre-screened units of human whole blood as well as animal blood. Stabilized RBC and Platelet pools and fixed erythrocytes (to simulate leukocytes) pools are manufactured independently. These pools are combined to provide the desired target ranges.	Same
Open Vial Stability	7 days when stored at 2-8°C	Same
Closed Vial Stability	120 days when stored at 2 - 8°C	Same

Differences		
<i>Item</i>	<i>COULTER® LIN-X Linearity Control (7 Levels)</i>	<i>COULTER® LIN-X Linearity Control (12 Levels)</i>
Final Product Form	Seven levels (Levels 1-7) Liquid, ready to use reagent.	Twelve levels (Levels 0-11) Liquid, ready to use reagent.

Differences		
Item	COULTER® LIN-X Linearity Control (7 Levels)	COULTER® LIN-X Linearity Control (12 Levels)
Analyzers	DxH™ 300 COULTER® Cellular Analysis System/DxH™ 300/300C COULTER® Cellular Analysis Systems	COULTER® LH 750, COULTER LH 780 and UniCel® DxH™ 800 COULTER® Cellular Analysis System

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

CLSI EP5-A2 *Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline – Second Edition*

L. Test Principle:

COULTER® LIN-X Linearity Controls are a hematology quality control material used to assess calibration and verify the reportable range of COULTER® Cellular Analysis Systems. The product’s WBC, RBC, HGB and PLT concentrations span the instrument reportable range. Results from repeated measurements for each concentration are compared to the established expected range to assess the instrument’s calibration and to verify the reportable range.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The precision performance of the LIN-X Linearity Control was evaluated on three lots of each of the seven levels which were run in triplicate, twice each day (AM and PM) for a minimum of 20 days on two DxH 300C and one DxH 300 analyzers. The results were analyzed according to the guidance provided in CLSI EP05-A2. Analysis was performed on each level of LIN-X Linearity Control (7 levels). Variance components were estimated for all sources of variability were controlled in the experiment based on a nested structure (lot, instrument, day, time within day, and repeatability). Repeatability variances of each site were checked for homogeneity before data from the three instruments were pooled together. The MIVQUE0 method was used for variance component estimation. Negative values of variance component estimates were defaulted to zero. Coefficients of variation (CV) were calculated for each source of variability. CV, reproducibility/repeatability and acceptance criteria are presented in the Tables below. The results met the acceptance criteria as indicated by the Repeatability/Reproducibility Specification.

Table 1: Precision Summary for Lin-X Level 1

Parameter	WBC	RBC	HGB	PLT
Mean	0.8	0.80	2.1	41
%CV				
Lot-to-Lot	6.7	2.0	3.9	0.0
Instrument-to-Instrument	0.4	0.5	0.8	4.3
Day-to-Day	0.0	0.2	0.4	0.7
Within day	0.0	0.4	0.2	0.7
Repeatability	3.9	1.4	0.7	5.0
Repeatability Specification	15.0	10.0	1.5	15.0

Reproducibility	7.8	2.5	4.0	6.7
Reproducibility Specification	17.0	12.0	6.0	18.0

Table 2: Precision Summary for Lin-X Level 2

Parameter	WBC	RBC	HGB	PLT
Mean	1.7	1.78	4.7	73
%CV				
Lot-to-Lot	2.7	0.6	2.5	0.0
Instrument-to-Instrument	0.2	0.9	0.9	4.0
Day-to-Day	0.0	0.2	0.1	0.0
Within day	0.7	0.5	0.4	1.0
Repeatability	2.6	1.0	0.5	3.9
Repeatability Specification	5.0	4.0	1.5	15.0
Reproducibility	3.8	1.5	2.7	5.7
Reproducibility Specification	10.0	5.0	6.0	18.0

Table 3: Precision Summary for Lin-X Level 3

Parameter	WBC	RBC	HGB	PLT
Mean	30.7	3.02	9.5	316
%CV				
Lot-to-Lot	4.9	1.2	0.0	0.0
Instrument-to-Instrument	0.1	0.7	0.7	3.9
Day-to-Day	0.4	0.0	0.0	0.5
Within day	0.1	0.5	0.4	0.4
Repeatability	0.9	0.9	0.5	2.0
Repeatability Specification	3.0	4.0	2.0	5.0
Reproducibility	5.0	1.7	1.0	4.4
Reproducibility Specification	6.0	5.0	6.0	13.0

Table 4: Precision Summary for Lin-X Level 4

Parameter	WBC	RBC	HGB	PLT
Mean	73.2	5.84	18.8	755
%CV				
Lot-to-Lot	1.2	0.2	0.4	0.0
Instrument-to-Instrument	0.5	0.4	0.5	3.9
Day-to-Day	0.1	0.1	0.2	0.0
Within day	0.6	0.7	0.6	0.9
Repeatability	0.8	1.0	0.7	1.7
Repeatability Specification	3.0	2.0	2.0	5.0
Reproducibility	1.6	1.4	1.2	4.3
Reproducibility Specification	6.0	5.0	6.0	13.0

Table 5: Precision Summary for Lin-X Level 5

Parameter	WBC	RBC	HGB	PLT
Mean	87.0	6.50	21.1	871
%CV				
Lot-to-Lot	1.7	0.6	0.5	0.0
Instrument-to-Instrument	0.8	0.2	0.6	3.8
Day-to-Day	0.0	0.0	0.0	0.0

Within day	0.8	0.9	0.8	1.1
Repeatability	0.7	1.0	0.6	1.6
Repeatability Specification	3.0	2.0	2.0	5.0
Reproducibility	2.2	1.5	1.2	4.2
Reproducibility Specification	6.0	5.0	6.0	13.0

Table 6: Precision Summary for Lin-X Level 6

Parameter	WBC	RBC	HGB
Mean	97.3	8.01	25.5
%CV			
Lot-to-Lot	1.6	0.0	0.0
Instrument-to-Instrument	1.6	0.7	1.2
Day-to-Day	0.0	0.0	0.0
Within day	1.1	1.3	1.1
Repeatability	1.1	1.5	0.9
Repeatability Specification	3.0	2.0	2.0
Reproducibility	2.7	2.1	1.9
Reproducibility Specification	6.0	5.0	6.0

Table 7: Precision Summary for Lin-X Level 7

Parameter	WBC	PLT
Mean	201.1	1976
%CV		
Lot-to-Lot	1.6	0.0
Instrument-to-Instrument	0.1	3.7
Day-to-Day	0.0	0.1
Within day	0.5	0.6
Repeatability	0.7	1.2
Repeatability Specification	3.0	5.0
Reproducibility	1.8	3.9
Reproducibility Specification	6.0	13.0

b. *Linearity/assay reportable range:*
Not applicable.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Value assignment: DxH™ 300 and DxH™ 300C hematology analyzer value assignments for each lot of LIN-X Linearity Control Levels 1 thru 7 are determined on validated systems using specific COULTER reagents. Approximately fifty (50) vials from each lot are taken randomly throughout the production run. For the value assignment process, two assay runs are required on two separate instruments and four to seven sample vials are analyzed for each assay run. An assay computer system is used to determine the number of replicates required for each assay run and analyze the data in real-time as the results are generated on the instrument system. A number of aspirations, sufficient to establish equivalence to the means, are taken for each assayed parameter. Once equivalence has been determined on the two separate assay runs, the assay value is calculated as the mean value of the two assay runs for each parameter. The difference between individual assay runs versus

the calculated assay value cannot exceed the established specification range for each of the parameters.

Open and Closed stability Three lots of **LIN-X Level 6 Linearity Control** samples were processed on both the DxH™ 300 and DxH™ 300C hematology analyzers according to the LIN-X Control package insert procedure. The testing was conducted throughout the proposed shelf life of 120 days at 2-8°C. The **Open Vial** stability was performed 7 times over the proposed shelf life. Two vials of each level of control were opened and tested 7 days, one vial on the open mode analyzer (DxH™ 300) and one on the closed mode (DxH™ 300C). The **Closed Vial** stability was performed twice a month over the proposed shelf life. Two vials of each level of control were run, one vial on the open mode analyzer (DxH™ 300) and one on the closed mode (DxH™ 300C). The mean of 5 aspirations for WBC Level 6 recovered values were compared to the assay values and the expected ranges established at the beginning of the test interval to assess the product's stability. A summary of the results for the stability data are as follows:

Table 1: LIN-X Level 6 WBC Open Vial Stability Summary Statistics

WBC Level 6			
	Set 3 Lot #661600	Set 4 Lot# 681700	Set 5 Lot# 681800
Mean	98.9	99.4	101.2
SD	3.3	3.4	3.7
%CV	3.3	3.4	3.6

Table 2: LIN-X Level 6 WBC Closed Vial Stability Summary Statistics

WBC Level 6			
	Set 3 Lot #661600	Set 4 Lot# 681700	Set 5 Lot# 681800
Mean	98.2	99.0	101.4
SD	3.1	3.7	3.4
%CV	3.2	3.7	3.3

Acceptance Criteria: WBC ± 12.0

Note: The stability of LIN-X Level 1-5 and Level 7 was previously cleared in k081641. There was no change in these six levels.

- 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:
The expected range for WBC Level 6 is calculated based on the other LIN-X ranges for DxH™ 300/300C Cellular Analysis System. The relationship between the target values and ranges for all levels is represented by a linear model. Verification of the expected ranges is conducted in a modality study on multiple analyzers. The estimated range for Level 6 is obtained from the regression line along with its 95% confidence limits. The upper confidence limit value of $\pm 12 \times 10^3$ cells/ μ L is the recommended range for Level 6. This expected range for Level 6 was established due to the addition of the WBC parameter.
The mean values of the all parameters should recover within the ranges provided. The ranges established by Beckman Coulter should be used as a guideline. Each laboratory must establish its own criteria for acceptable results.

N. Proposed Labeling:

The labeling is sufficient and it 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.