

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

**A. 510(k) Number:**

k100607

**B. Purpose for Submission:**

Addition of a new parameter - RDW-SD (Red Cell Distribution Width-Standard Deviation) to the COULTER® 4C®-EX 300 Cell Control.

**C. Measurand:**

WBC, RBC, Hgb, Hct, MCV, MCH, MCHC, RDW, RDW-SD, Plt, MPV and [LY (%/#), MO (%/#), GR (%/#)].

**D. Type of Test:**

Quantitative

**E. Applicant:**

Beckman Coulter, Inc.

**F. Proprietary and Established Names:**

COULTER® 4C®-EX 300 Cell 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:

Hematology (81)

**H. Intended Use:**

1. Intended use(s):

4C®-EX 300 Cell Control is a hematology quality control material used to monitor the performance of COULTER® hematology analyzers listed in the TABLE OF EXPECTED RESULTS in conjunction with specific COULTER reagents (Refer to your instrument specific instructions for use).

The assigned values and expected ranges on the TABLE OF EXPECTED RESULTS can be used to monitor instrument performance. This product can also be used to establish your own laboratory mean.

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 Coulter DxH™ 300 and DxH™ 300C analyzers

**I. Device Description:**

4C®-EX 300 Cell Control is a hematology quality control mixture intended to be used with automated cell and differential cell counters. It is prepared from stabilized human blood so that repeated measurements by an automated cell or differential cell counter can be made to monitor instrument daily performance. 4C®-EX 300 Cell

Control consists of treated, stabilized human erythrocytes, a stabilized platelet sized component, and fixed erythrocytes that simulate leukocytes. Three levels of varying component concentrations (Abnormal Low, Abnormal High, and Normal) are offered.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
COULTER® 4C®-ES Cell Control
2. Predicate 510(k) number(s):  
k010064
3. Comparison with predicate:

<b>Similarities</b>		
Item	4C®-EX 300 Cell Control	4C®-ES Cell Control
Product Description	Consists of treated, stabilized human erythrocytes in an isotonic medium. It also contains a stabilized platelet-sized component, and fixed erythrocytes to simulate leukocytes.	Same
Intended Use	A hematology quality control material used to monitor the performance of Beckman Coulter instruments listed in the Table of Expected Results in conjunction with specific Coulter reagents (Refer to your instrument specific instructions for use). The assigned values and expected ranges on the Table of Expected Results can be used to monitor instrument performance. This product can also be used to establish your own laboratory mean.	Same
Cellular Populations	White blood cells (Leukocytes), Red blood cells (Erythrocytes), Platelets, Lymphocytes, Monocytes, and Granulocytes	Same
Assayed Parameters	WBC, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, RDW-SD, PLT, MPV, LY%, MO%, GR%, LY#, MO#, GR#.	Same except RDW-SD
Final Product Form	Three levels. Liquid, ready to use reagent.	Same
Open Vial Stability	20 events over 35 days when stored at 2 - 8°C.	Same

<b>Differences</b>		
Item	4C®-EX 300 Cell Control	4C®-ES Cell Control
Closed Vial Stability	145 days when stored at 2 - 8°C	154 days when stored at 2 - 8°C.
Analyzers	DxH™ 300 COULTER® Cellular Analysis System/DxH™ 300C COULTER® Cellular Analysis System capable of analyzing the RDW-SD parameter.	ONYX™, ONYX™ with Autoloader, MD™ Series, MD™ II, Ac•T™ 8/10, Ac•T diff™, Ac•T diff2™, JT™, JT2, JT3 and T Series.

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

CLSI EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition

CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline

**L. Test Principle:**

COULTER® 4C®- EX 300 Cell Control is a reference product prepared from stabilized human blood cells. 4C®- EX 300 Cell Control confirms and monitors instrument accuracy and precision performance by providing measurements for counting, sizing and hemoglobin determination.

**M. Performance Characteristics (if/when applicable):**1. Analytical performance:a. *Precision/Reproducibility:*

Two separate studies demonstrate the precision/reproducibility of the DxH 300/300C systems.

Study 1: One lot of each level of 4C-EX 300 Cell Control (Abnormal Low, Normal and Abnormal High) was run in duplicate twice each day for a minimum of 20 days on the DxH 300 and DxH 300C analyzers at three test sites. The results were analyzed according to the guidance provided in CLSI EP05-A2. Variance components were estimated for all sources of variability controlled in the experiment based on a nested structure (site, day-within site, within day, and repeatability). Negative values of variance component estimates were defaulted to zero. The individual results are compared against the repeatability/reproducibility specifications. The results met the acceptance criteria as displayed in the tables below.

## 4C-EX 300 Cell Control Precision Abnormal Low Level

DxH 300C							
Parameter	Mean	CV%					
		Site/Instrument	Day	Within Day	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	3.8	2.1	1.0	0.8	8.0	2.0	5.0
RBC	2.47	3.5	0.5	1.1	6.2	0.9	4.0
HGB	6.8	1.0	0.7	0.7	6.4	0.7	1.5
HCT	19.5	4.7	0.0	1.3	N/A	0.9	N/A
MCV	79.1	1.2	0.1	0.3	3.4	0.2	1.0
MCH	27.6	2.7	0.0	0.7	N/A	0.8	N/A
MCHC	34.8	3.9	0.0	0.7	N/A	0.8	N/A
RDW	13.7	1.0	1.1	0.9	12.4	1.6	3.5
RDW-SD	40.7	1.7	0.9	0.8	13.7	1.4	3.5
PLT	78	3.6	3.0	1.1	18.8	4.4	15.0
MPV	9.9	2.6	1.1	0.0	9.4	2.4	3.0
LY%	34.2	1.1	1.0	1.1	12.0	3.3	4.4
MO%	12.5	1.0	2.3	2.6	21.4	5.6	24.1
GR%	53.3	0.5	0.0	0.6	6.8	1.9	5.6
LY#	1.3	1.2	1.6	0.8	N/A	4.4	N/A
MO#	0.5	3.3	3.5	0.0	N/A	8.5	N/A
GR#	2.0	2.2	0.8	0.6	N/A	3.8	N/A

DxH 300							
Parameter	Mean	CV%					
		Site/Instrument	Day	Within Day	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	3.8	2.4	1.4	0.0	8.0	2.2	5.0
RBC	2.49	2.5	0.7	0.9	6.2	0.8	4.0
HGB	6.8	1.3	0.8	0.4	6.4	0.8	1.5
HCT	19.7	2.9	0.3	1.0	N/A	0.9	N/A
MCV	79.1	0.8	0.1	0.3	3.4	0.2	1.0
MCH	27.2	3.2	0.0	0.6	N/A	0.7	N/A
MCHC	34.4	3.8	0.0	0.8	N/A	0.8	N/A
RDW	13.7	1.1	0.5	1.1	12.4	1.7	3.5
RDW-SD	40.3	0.9	0.0	0.9	13.7	1.6	3.5
PLT	80	3.2	5.6	1.8	18.8	4.1	15.0
MPV	9.9	1.9	0.0	0.0	9.4	2.8	3.0
LY%	34.5	0.4	0.0	1.6	12.0	3.3	4.4
MO%	12.4	0.0	2.1	0.5	21.4	5.8	24.1
GR%	53.2	0.2	0.3	0.7	6.8	1.8	5.6
LY#	1.3	2.4	1.3	1.7	N/A	4.4	N/A
MO#	0.5	2.9	2.5	0.0	N/A	9.2	N/A
GR#	2.0	2.2	1.3	0.0	N/A	3.7	N/A

#### 4C-EX 300 Cell Control Precision Normal Level

DxH 300C							
Parameter	Mean	CV%					
		Site/Instrument	Day	Within Day	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	8.7	2.4	0.6	0.9	4.9	1.4	3.0
RBC	4.17	3.0	0.0	1.3	3.6	0.6	2.0
HGB	12.9	0.3	0.8	0.8	4.3	0.8	1.5
HCT	36.8	4.2	0.0	1.5	N/A	0.2	N/A
MCV	88.2	1.2	0.0	0.4	3.1	0.1	1.0
MCH	31.0	2.8	0.0	0.8	N/A	0.5	N/A
MCHC	35.2	4.0	0.0	1.1	N/A	0.0	N/A
RDW	12.0	0.6	0.1	0.5	12.7	1.1	3.5
RDW-SD	41.6	1.3	0.5	0.3	13.6	1.3	3.5
PLT	224	3.8	2.2	0.0	15.4	2.5	5.0
MPV	10.3	2.6	0.9	0.0	12.6	1.1	3.0
LY%	45.8	0.7	0.7	0.0	6.6	1.8	3.3
MO%	12.8	1.5	1.3	0.0	18.1	4.0	23.4
GR%	41.5	0.7	0.6	0.0	9.0	1.6	7.2
LY#	4.0	1.9	1.3	1.0	N/A	2.6	N/A

MO#	1.1	2.5	0.6	0.0	N/A	5.4	N/A
GR#	3.6	3.0	1.1	0.0	N/A	2.4	N/A
DxH 300							
Parameter	Mean	CV%					
		Site/Instrument	Day	Within Day	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	8.7	2.3	1.0	0.3	4.9	1.4	3.0
RBC	4.19	2.1	0.8	0.6	3.6	0.8	2.0
HGB	12.9	1.3	0.7	0.4	4.3	0.6	1.5
HCT	37.0	2.6	0.6	0.8	N/A	0.8	N/A
MCV	88.3	0.8	0.0	0.3	3.1	0.1	1.0
MCH	30.5	3.0	0.0	0.6	N/A	0.8	N/A
MCHC	34.9	3.6	0.0	0.8	N/A	0.7	N/A
RDW	12.0	0.8	0.5	0.0	12.7	1.0	3.5
RDW-SD	41.4	1.2	0.4	0.0	13.6	1.2	3.5
PLT	227	2.9	3.0	0.4	15.4	2.9	5.0
MPV	10.3	2.0	0.9	0.4	12.6	1.0	3.0
LY%	45.9	0.3	0.7	0.5	6.6	1.7	3.3
MO%	12.8	0.1	1.8	0.0	18.1	4.4	23.4
GR%	41.3	0.3	0.5	0.8	9.0	1.4	7.2
LY#	4.0	2.5	1.2	0.1	N/A	2.4	N/A
MO#	1.1	1.6	1.3	0.0	N/A	5.3	N/A
GR#	3.6	2.3	1.3	1.1	N/A	2.1	N/A

#### 4C-EX 300 Cell Control Precision Abnormal High Level

DxH 300C							
Parameter	Mean	CV%					
		Site/Instrument	Day	Within Day	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	18.0	2.3	0.9	0.9	4.0	0.9	3.0
RBC	5.34	2.8	0.7	0.8	3.4	0.8	2.0
HGB	18.3	0.7	0.7	0.8	3.1	0.5	1.5
HCT	51.6	4.1	0.5	0.9	N/A	0.7	N/A
MCV	96.7	1.3	0.0	0.3	3.1	0.0	1.0
MCH	34.3	2.3	0.0	0.4	N/A	0.7	N/A
MCHC	35.5	3.6	0.0	0.4	N/A	0.6	N/A
RDW	11.6	0.5	0.4	0.5	13.2	0.8	3.5
RDW-SD	44.2	1.5	0.6	0.6	14.3	1.2	3.5
PLT	436	4.5	1.5	1.3	11.4	1.5	5.0
MPV	10.3	2.8	0.8	0.0	12.4	0.7	3.0
LY%	50.5	0.7	0.4	0.3	6.1	1.1	5.9
MO%	15.7	1.4	0.7	0.5	18.3	2.6	19.1

GR%	33.8	0.7	0.2	0.0	9.1	1.3	8.9
LY#	9.1	2.1	1.0	0.7	N/A	1.6	N/A
MO#	2.8	2.3	1.2	0.8	N/A	2.6	N/A
GR#	6.1	2.9	0.8	1.2	N/A	1.6	N/A
DxH 300							
Parameter	Mean	CV%					
		Site/Instrument	Day	Within Day	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	18.0	2.4	0.8	0.7	4.0	0.8	3.0
RBC	5.34	1.9	0.8	0.8	3.4	0.8	2.0
HGB	18.2	1.5	0.6	0.5	3.1	0.5	1.5
HCT	51.6	2.4	0.8	0.8	N/A	0.7	N/A
MCV	96.7	0.8	0.1	0.2	3.1	0.2	1.0
MCH	34.0	3.1	0.0	1.2	N/A	0.7	N/A
MCHC	35.2	3.7	0.0	0.6	N/A	0.6	N/A
RDW	11.7	0.0	0.7	0.0	13.2	0.9	3.5
RDW-SD	44.0	0.6	0.8	0.0	14.3	1.3	3.5
PLT	443	2.9	2.8	1.4	11.4	1.8	5.0
MPV	10.3	2.2	1.0	0.4	12.4	0.7	3.0
LY%	50.6	0.5	0.5	0.5	6.1	1.0	5.9
MO%	15.7	1.1	1.3	0.0	18.3	2.3	19.1
GR%	33.7	0.3	0.2	0.5	9.1	1.2	8.9
LY#	9.1	2.5	0.7	0.8	N/A	1.5	N/A
MO#	2.8	2.4	1.4	0.9	N/A	2.5	N/A
GR#	6.1	2.5	1.0	1.0	N/A	1.6	N/A

Study 2: An analysis of a subset of the 4C-EX 300 Cell Control stability data was performed to assess the precision/reproducibility of multiple lots of the product over time. The data was collected, and included three lots of each level of 4C-EX Cell Control (Abnormal Low, Normal and Abnormal High). For each lot, five replicates per day for a total of four days were obtained on one DxH 300 and one DxH 300C analyzers. The analysis of all the lots spanned throughout approximately 45 days. All sources of variability were considered to be random. The estimates with negative values were defaulted to zero. The individual results are compared against the repeatability/reproducibility specifications. The results met the acceptance criteria as displayed in the tables below.

#### 4C-EX 300 Cell Control DxH 300/300C Precision Abnormal Low Level

Parameter	Mean	CV%					
		Day	Instrument	Lot	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	3.7	1.6	2.5	3.1	8.0	2.3	5.0
RBC	2.46	0.0	2.3	3.4	6.2	1.2	4.0
HGB	6.6	0.0	1.4	3.4	6.4	0.7	1.5

HCT	19.6	0.0	2.7	4.4	N/A	1.3	N/A
MCV	79.9	0.0	0.4	1.1	3.4	0.2	1.0
MCH	26.9	0.0	1.1	0.5	N/A	1.1	N/A
MCHC	33.6	0.0	1.4	1.2	N/A	1.1	N/A
RDW	12.3	2.0	1.3	1.8	12.4	1.4	3.5
RDW-SD	37.1	1.4	1.5	2.4	13.7	1.4	3.5
PLT	72.6	0.0	3.7	2.4	18.8	3.3	15.0
MPV	10.0	1.4	0.8	1.8	9.4	2.2	3.0
LY%	35.2	0.7	1.1	1.2	12.0	3.5	4.3
MO%	11.6	6.2	0.8	6.9	21.4	5.3	25.9
GR%	53.2	2.3	0.7	2.0	6.8	2.3	5.6
LY#	1.3	3.2	2.9	3.5	N/A	3.8	N/A
MO#	0.4	8.2	1.5	9.6	N/A	5.6	N/A
GR#	2.0	0.0	2.7	2.3	N/A	3.7	N/A

#### 4C-EX 300 Cell Control DxH 300/300C Precision Normal Level

Parameter	Mean	CV%					
		Day	Instrument	Lot	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	8.5	0.0	3.3	2.0	4.9	1.1	3.0
RBC	4.20	0.0	2.1	0.6	3.6	1.1	2.0
HGB	12.6	0.0	1.1	0.5	4.3	0.6	1.5
HCT	37.1	0.0	2.4	0.7	N/A	1.1	N/A
MCV	88.4	0.0	0.5	0.8	3.1	0.2	1.0
MCH	29.9	0.0	1.1	0.7	N/A	1.0	N/A
MCHC	33.9	0.0	1.4	1.1	N/A	1.0	N/A
RDW	12.0	0.0	0.8	1.2	12.7	1.2	3.5
RDW-SD	40.4	0.0	1.6	1.8	13.6	1.5	3.5
PLT	217.7	0.0	3.0	1.2	15.4	2.4	5.0
MPV	10.0	1.1	0.4	0.8	12.6	0.8	3.0
LY%	45.6	0.0	0.7	0.6	6.6	1.7	3.3
MO%	13.7	1.7	2.5	3.2	18.1	3.6	21.9
GR%	40.7	0.9	0.6	1.5	9.0	1.6	7.4
LY#	3.9	0.0	3.9	2.5	N/A	1.7	N/A
MO#	1.2	3.8	0.0	4.9	N/A	4.1	N/A
GR#	3.5	0.0	3.7	0.4	N/A	2.0	N/A

#### 4C-EX 300 Cell Control DxH 300/300C Precision Abnormal High Level

Parameter	Mean	CV%					
		Day	Instrument	Lot	Reproducibility Specification	Repeatability	Repeatability Specification
WBC	18.2	0.0	3.6	1.9	4.0	1.0	3.0

RBC	5.34	0.0	1.7	0.7	3.4	1.1	2.0
HGB	17.7	0.0	0.9	0.5	3.1	0.5	1.5
HCT	51.8	0.0	2.1	1.3	N/A	1.0	N/A
MCV	97.0	0.0	0.5	0.7	3.1	0.2	1.0
MCH	33.2	0.0	1.1	0.6	N/A	0.9	N/A
MCHC	34.2	0.0	1.4	1.3	N/A	0.9	N/A
RDW	11.6	0.5	0.3	0.6	13.2	0.8	3.5
RDW-SD	42.9	0.0	2.0	1.4	14.3	1.1	3.5
PLT	436.9	0.0	3.4	1.3	11.4	1.9	5.0
MPV	10.2	2.6	0.3	2.1	12.4	0.7	3.0
LY%	49.7	0.0	0.1	0.3	6.1	1.0	6.0
MO%	16.7	0.6	1.2	1.0	18.3	2.3	18.0
GR%	33.7	0.6	0.0	0.6	9.1	1.1	8.9
LY#	9.0	0.0	3.8	1.8	N/A	1.5	N/A
MO#	3.0	2.4	2.2	2.8	N/A	2.3	N/A
GR#	6.1	0.0	3.7	1.7	N/A	1.5	N/A

b. *Linearity/assay reportable range:*

Not applicable.

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

Value assignment: 4C®- EX 300 Cell Control assigned values are determined on validated systems using specific Beckman Coulter reagents. One hundred (100) 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. 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. Zero biased, equilibration adjusted data and the raw data from the instrument assay run data is used to determine the final value assignment. The value assignments are confirmed by performing a verification test of the product on the instruments for which the cell control is intended to be used.

Open and Closed Vial Stability: Three lots of each level (Abnormal Low, Normal, and Abnormal High) were processed on both DxH™ 300 and DxH™ 300C analyzers. Testing was conducted throughout the proposed shelf life. Open Vial Stability was determined to be 20 events over 35 days when stored at 2 - 8°C. Closed Vial Stability was determined to be 145 days when stored at 2 - 8°C. The RDW-SD recovered values were compared to assay values established at the beginning of the test interval and the expected ranges to assess the product's stability.

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 ranges for RDW-SD were calculated based upon the assigned values and expected ranges of MCV and RDW parameters, and the mathematical relationship between these parameters for each level of 4C®- EX 300 Cell Controls. This methodology allows for the preservation of the same variability built in the MCV and RDW specifications. The expected ranges are provided in the Table of Expected 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.