510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
K040898

B. Purpose for Submission:
New device

C. Analyte:
Circulating Breast Epithelial Tumor Cells

D. Type of Test:
Quality Control Material

E. Applicant:
Veridex, LLC (Johnson and Johnson Company)

F. Proprietary and Established Names:
CellSearch™ Epithelial Cell Control Kit

G. Regulatory Information:

1. Regulation section:
   21 CFR 864.8625
2. Classification:
   Class II
3. Product Code:
   NRS
4. Panel:
   Hematology Panel

H. Intended Use:

5. Intended use(s):
   The CellSearch™ Epithelial Cell Control Kit is intended for use as an assay control to ensure that the sample detection and identification systems are working when performing the CellSearch™ Assay.
6. Indication(s) for use:
   A CellSearch™ Epithelial Cell Control bottle is substituted for a patient sample to verify the performance of the CellSearch™ Epithelial Cell Kit reagents; sample processing by the CellTracks® AutoPrep System; and cell analysis by the CellSpotter® Analyzer.
7. Special condition for use statement(s):
   For prescription use only
8. Special instrument Requirements:

To be used with the CellTracks® AutoPrep System and the CellSpotter® Analyzer.

I. Device Description:

The CellSearch Epithelial Cell Control Kit contains single-use vials of fixed cells from the breast carcinoma cell line SKBR-3. Each vial contains two populations of the SKBR-3 cells at different concentrations, low and high, which are distinguished from each other by use of fluorescent dyes that are specific for each population. Stability studies have been performed for shelf life; there is no need for open vial studies because the control is single use. The shelf-life is 9 months at 4^0C.

H. Substantial Equivalence Information:

1. Predicate device name(s):
   Control Cell Kit cleared with the CellSearch CellSpotter
2. Predicate K number(s):
   K031588
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Indications for Use	The CellSearch™ Epithelial Cell Control Kit is intended for use as an assayed control when running the CellSearch™ Epithelial Cell Kit on the CellSpotter® Analyzer/Cell Tracks® AutoPrep System to ensure the sample detection and identification systems are able to detect circulating tumor cells.	The Control Cell Kit is for use as an assay control when running the CellSearch™ assay to ensure that the sample detection and identification systems are working.
Cells	Breast Cancer Cell Line (SKBr-3)	Same
Fixative	Paraformaldehyde	Same
Dyes used to pre-label cells	DiOC16(3) for high control cell population.	Same
Control Matrix Ingredient	5% Bovine Serum Albumin, 0.1% Sodium Azide	Same
Differences		
Item	**Device**	**Predicate**
Control Matrix Ingredient	Histopaque 1083	Phosphate Buffered Saline
Control Cell levels; Expected Target Values	Two populations of cells: High (1000 cells/test); Low (50 cells/test)	One population of cells: High (1000 cells/test)

Dyes used to pre-label cells	DiIC18(5) for low control cell population	None
Tests/vial	Unit dose (one test/vial); 24 tests per kit	10 tests/vial; 10 tests per kit

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

● Guidance for FDA Reviewers and Industry for the Content of Premarket Submissions (draft:3 August 1999)

● In Vitro Diagnostic Devices: Guidance for the Preparation of 510(k) Submission (January 1997)

● Medical Devices-Risk Management Part 1: Application of Risk Analysis, International Standards Organization, ISO 14971-1:1998 (E)

● Guidance for Industry. Points to Consider Guidance Document on Assayed and Unassayed Quality Control Materials.

● Points to Consider for Hematology Quality Control Materials. September 30, 1997.

J. Test Principle:

Each single use vial in the CellSearch™ Epithelial Cell Control Kit contains two populations of SKBR-3 cells at different concentrations (low and high). The two cell populations are distinguished from each other by use of different fluorescent dyes that are specific for each population. This permits simultaneous enumeration of low and high control cells by the CellSpotter® Analyzer. The CellSearch™ Epithelial Cell Control Kit with its pre-stained and fixed control cells are automatically identified as CTCs (circulating tumor cells) by the system. They are magnetically captured by the CellSpotter® Analyzer and acquired as images that are displayed to the user for final classification, thus providing a model system to evaluate the process.

Performance Characteristics (if/when applicable):

4. <u>Analytical performance:</u>

a. Precision/Reproducibility:

● A 20-day precision study was performed according to NCCLS EP-5A, *Evaluation of Precision Performance of Clinical Chemistry Devices* running duplicate control cell samples in the morning and afternoon each day at two sites. The total imprecision (%CV) for the High Control cells from Immunicon and an external site are 6.39 and 5.11 respectively. The acceptance range for these lot specific control cells was 939 to 1335 for the High Control and 22 to 81 for the Low Control. The count for both sites were within the acceptance ranges except for two tests where the High Control counts were below the acceptance number (2/80 = 2.5%). The reason for the outliers could not be determined, but they did not repeat.

● A system performance verification study was performed at three sites with three CellTrack® AutoPrep Systems and three CellSpotter® Analyzers, using two CellSearch™ Epithelial Control samples that were

run per instrument twice a day over a 39-day period. The results of within-run and total precision standard deviation and %CV for each instrument, as well as combined are presented in the following table:

Estimates of Within-Run and Total Precision

AutoPrep I.D.	# of Days	Estimate of Within-Run Precision				Estimate of Total Precision			
		Std. Deviation		% CV		Std. Deviation		% CV	
		Low	High	Low	High	Low	High	Low	High
P8	20	7	51	14%	5%	7	50	15%	4%
P9	20	8	57	17%	5%	7	57	15%	5%
P10	20	9	55	17%	5%	8	61	16%	5%
Overall	60	8	54	16%	5%	8	56	15%	5%

The range of recoveries for each instrument control cell runs is listed in the table below.

Range and Averages of Control Cell Recoveries

Control Cells	P8		P9		P10		Overall	
Statistic	Low	High	Low	High	Low	High	Low	High
Minimum	34	984	33	993	28	955	28	955
Maximum	66	1224	68	1290	71	1261	71	1290
Average	51	1113	49	1111	51	1125	50	1116

The average recoveries of the high and low control cells and CV of the duplicates are presented in the table below.

Average Recoveries and CV of the Low and High Control Cell Duplicates

AutoPrep I.D.	# of Control Runs	Control #1 Average Results		Control #2 Average Results		All Control Runs						Overall Average %CV
						Average		Std. Deviation		% CV		
		Low	High	Low	High	Low	High	Low	High	Low	High	
P8	40	52	1108	49	1118	51	1113	5	40	11%	4%	7%
P9	40	48	1118	50	1104	49	1111	7	44	13%	4%	9%
P10	40	50	1124	52	1126	51	1125	7	44	13%	4%	9%
Overall	120	50	1117	50	1116	50	1116	6	43	13%	4%	8%

● A variability study with day-to-day; operator-to-operator; and instrument to instrument testing was performed. The study used three operators and three instruments over three days with two lots of control cells. The results are shown in the following tables.

Lot 1 Performance Summary Data

A: High Control Cells

Operator	Instru-ment	Day 1			Day 2			Day 3			Overall		
		Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV
Oper#1	**P5**	971	40	4.1	984	46	4.6	975	29	2.9	977	38	3.9
Oper#2	**E3**	962	30	3.1	939	58	6.1	933	55	5.8	945	49	5.2
Oper#3	**E6**	996	25	2.5	962	63	6.5	1010	47	4.6	989	50	5.0

B: Low Control Cells

Operator	Instrument	Day 1			Day 2			Day 3			Overall		
		Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV
Oper#1	**P5**	46	8	17.3	46	6	13.0	48	6	12.5	47	7	14.6
Oper#2	**E3**	43	10	23.2	44	8	18.1	44	7	15.9	44	8	18.3
Oper#3	**E6**	53	5	9.4	46	7	15.2	47	9	19.1	49	8	15.6

Lot 2 Performance Summary Data

A: High Control Cells

Operator	Instrument	Day 1			Day 2			Day 3			Overall		
		Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV
Oper#1 (CCR)	**P9**	1145	79	6.8	1134	40	3.5	1136	52	4.5	1139	57	5.0
Oper#2 LMW	**P10**	1184	27	2.2	1134	55	4.8	1158	54	4.6	1158	50	4.3
Oper#3 GM	**E6**	1153	60	5.2	1114	15	1.3	1086	15	1.3	1117	52	4.7

B: Low Control Cells

Operator	Instrument	Day 1			Day 2			Day 3			Overall		
		Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV	Ave.	S.D.	%CV
Oper#1 (YY)	**P5**	51	7	13.7	50	8	16.0	51	6	11.7	51	7	13.4
Oper#2 MH	**E3**	50	7	14.0	56	11	19.6	50	8	16.0	52	9	17.5
Oper#3 CCR	**E6**	57	7	12.2	50	7	14.0	50	7	14.0	52	9	17.5

b. Linearity/assay reportable range:
Not applicable

c. Traceability (controls, calibrators, or method):
Not applicable.

d. Detection limit:
Not applicable.

e. Analytical specificity:
Not applicable

f. Assay cut-off:
Not applicable

5. Comparison studies:
   a. Method comparison with predicate device:
   Not available
   Matrix comparison:
   The new Epithelial Cell Control is in a matrix consisting of Histopaque 1083; 5% Bovine Serum Albumin; and 0.1% sodium azide while the patient samples will be epithelial cells from whole blood. A matrix effects study was performed with the Control cells spiked into either the Control Cell Product Matrix or whole blood. Both samples were processed on the CellTrack® AutoPrep System and CellSpotter® Analyzer. The results indicate that at the low-end cell concentration, the means differed by only 1 cell between matrices and at the high-end cell concentration, the means differed by 67 cells; this difference for the high-end cell concentration is small but statistically significant. Data is in table below.

Results of Control Cells Spiked into Product Matrix or Whole Blood

Sample Number	Low Control Cell Population		High Control Cell Population	
	Whole Blood	Control Cell Matrix	Whole Blood	Control Cell Matrix
1	67	43	740	754
2	47	43	809	802
3	36	30	763	799
4	35	42	767	873
5	41	46	754	887
6	35	33	808	849
7	42	56	775	885
8	34	37	763	866
Mean	**42**	**41**	**772**	**839**
Std. Dev.	11	8	25	49
% CV	26.2%	19.5%	3.2%	5.8%
t-test p-value	0.859		0.004	

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):
   None provided
4. Clinical cut-off:
   Not applicable.

5. Expected values/Reference range:
   Not applicable

Conclusion:

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