510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k072901

B. Purpose for Submission:
New device

C. Measurand:
Fibrin and Fibrinogen Degradation Products (FDP)

D. Type of Test:
Quantitative, ELISA Immunoassay

E. Applicant:
AMDL Inc.

F. Proprietary and Established Names:
DR-70® FDP

G. Regulatory Information:

1. Regulation section:
   21 CFR §866.6010, Tumor associated antigen immunological test system
2. Classification:
   Class II
3. Product codes:
   NTY, System, Test, Fibrin/Fibrinogen degradation products for monitoring of colorectal cancer
4. Panel:
   Immunology (82)

H. Intended Use:

1. Intended use:
   The DR-70® (FDP) ELISA is designed for IN VITRO DIAGNOSTIC USE ONLY for the quantitative measurement of DR-70® (FDP) in human serum.
2. Indication(s) for use:
   Serial testing using the AMDL-ELISA DR-70® (FDP) is to be used as an aid in monitoring the disease progression of patients who have been diagnosed previously with colorectal cancer. Results of DR-70® (FDP) testing should be used in conjunction with other clinical modalities that are standard of care for monitoring disease progression in these patients.
3. Special conditions for use statement(s):
   For prescription only.
4. Special instrument requirements:
   ELISA microwell plate reader that reads the 450 nm (kinetic) wavelengths

I. Device Description:
The DR-70® (FDP) Kit consists of DR-70® (FDP) Antibody-Coated Wells for a 96-well Plate); Enzyme Antibody Conjugate; Low Control; High Control; DR-70® (FDP) calibrators at concentrations of: 0, 0.625, 2.5, 5.0, and 10.0 µg/mL; Diluent Buffer Concentrate (5X): Wash Buffer Concentrate (20X): 3,3',5,5'-tetramethylbenzidine (TMB) Substrate; Stop Solution and Dilution/Transfer Plate (96 well uncoated Plate)

J. Substantial Equivalence Information:

1. Predicate device name(s):
   TOSOH BioScience AIA-PACK™ CEA
2. Predicate K number(s):
   P910053
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	AMDL-ELISA DR-70®(FDP)	TOSOH AIA-PACK™ CEA
Intended Use	Monitoring disease progression in patients previously diagnosed with colorectal cancer	Same
Sample	Human serum	Same

Differences		
Item	New Device	Predicate Devices
	AMDL-ELISA DR-70®(FDP)	TOSOH AIA-PACK™ CEA
Analytes	Fibrin and Fibrinogen Degradation products	Cancer Embryonic Antigen (CEA)
Antibody	Polyclonal (rabbit)	Monoclonal (mouse)
Methodology	Manual ELISA	Automated Immunoassay analyzers
Solid phase capture	Antibody-coated microwells	Antibody-coated magnetic beads
Substrate	TMP	4-methylumbelliferyl phosphate
Detection Method	Chromogenic	Fluorogenic
Precision	< 10.6%	3.2-3.9%
Sample Volume	100 µL	10 µL

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

CLSI EP5-A2 for precision study; EP6A for linearity.

L. Test Principle:

The AMDL, Inc. DR-70® (FDP) assay is an ELISA based assay utilizing removable strips in a 96 micro titer plate well format. The wells are coated with affinity purified rabbit anti-DR-70 polyclonal antibodies. The DR-70 antigen in diluted patient serum (1:200) is captured by these antibodies immobilized in the well of a micro titer plate. After a wash step, anti-DR-70 antibodies conjugated to horseradish peroxidase (HRP) are added to the wells. If the DR-70 antigen is present, the HRP-labeled anti-DR-70 Ab will bind to the captured tumor marker to form an immunological sandwich with the immobilized antibodies.

After a second wash step, the enzyme substrate TMB is added to the well. The end point is read in a micro plate reader at 450 nm once the reaction is stopped with 0.1N HCl. The intensity of the color formed is proportional to the amount of DR-70 in the serum. The amount is quantified by interpolation from a standard curve using the calibrators provided with the kit.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Five specimens were tested by 3 sites, 20 days, 3 lots, 2 runs (per day), and replicate (2 per run) for 720 lines of data per specimen. The five specimens were Pool 1 (low concentration), Pool 2 (medium concentration), Pool 3 (high concentration), QC1 (low concentration), and QC2 (high concentration). The study day is nested within study site and run is nested within day. To obtain variance components for all variables, each was considered random in the mixed model.

The highest mean concentration of serum pool for the precision study of 2.8 ng/mL is accepted based on the rationales that majority (>90%) of observed FDP of colorectal cancer are below 5 ng/mL, and the assay imprecision is usually lower in the upper assay range.

Table 1: Intra-assay, Between-run, Day-to-day, and Total Assay Imprecision

Sample	Mean Concentration (µg/mL)	Within-Site Imprecision (%CV)	Between-Day Imprecision (%CV)	Between-Lot Imprecision (%CV)	Within-Run Imprecision (%CV)	Total Variability (%CV)
Pool 1	0.315	11.60	6.48	6.64	5.53	22.53
Pool 2	1.389	3.51	4.31	0.83	3.06	10.60
Pool 3	2.739	4.45	3.43	0.76	2.74	9.91
QC 1	0.240	13.74	8.58	11.03	4.84	28.21
QC 2	2.994	5.01	3.74	3.05	1.27	11.8

Table 2. Total and Components of Assay Variance and Percentage by Source

Specimen	Mean Concentration (µg/mL)	**Site Variance (%)**	**Day Variance (%)**	**Lot Variance (%)**	**Run Variance (%)**	**Residual Variance (%)**	**Total Variance**
Pool 1	0.315	0.001336 (23.53)	0.000417 (8.28)	0.000437 (8.68)	0.000303 (6.02)	0.002543 (50.50)	0.005036
Pool 2	1.389	0.002385 (11.00)	0.003585 (16.53)	0.000132 (0.61)	0.001810 (8.34)	0.01378 (63.53)	0.021692
Pool 3	2.739	0.01483 (20.11)	0.008803 (11.94)	0.000431 (0.58)	0.005631 (7.64)	0.04405 (59.73)	0.073745
QC1	0.240	0.001088 (23.74)	0.000424 (9.25)	0.000701 (15.29)	0.000135 (2.95)	0.002236 (48.78)	0.004584
QC2	2.994	0.02246 (20.03)	0.01255 (11.19)	0.008363 (7.46)	0.001438 (1.28)	0.06731 (60.03)	0.112121

Accuracy/Spiked Recovery

Sera from three normal subjects having DR-70 values ranging from 0.3 µg/mL to

0.6 µg/mL and a control diluent buffer were spiked with a DR-70 antigen solution to obtain expected levels ranging from 1.5 µg/mL to 10 µg/mL to represent the range of the DR-70 calibrators. The values of DR-70 in the spiked serum samples were measured and compared to the theoretical values and to values obtained for the control diluent buffer. The experiment was designed to compare responses of the analyte in a biological sample versus the standard diluent to assess for any difference in assay response.

Table 3. Spike Recovery

Sample	Non-spiked	Spiked in DR-70 concentration value (µg/mL)				
		1.5	2.5	5.0	7.0	10
Diluent buffer(5x)	0	1.517	2.649	4.586	6.983	10.94
Patient 1	0.428	1.743	2.908	4.839	7.057	13.11
Patient 2	0.576	1.520	2.680	4.848	7.050	11.95
Patient 3	0.464	1.598	2.967	5.193	6.701	10.88
Patient mean value	0.489	1.620	2.852	4.960	6.936	11.98
% Mean Recovery	-----	107%	108%	108%	99%	110%

b. *Linearity/assay reportable range*

Linearity

The linearity of a marker over the range of evaluation was analyzed by a method consistent with NCCLS EP6-A. Two-fold serial dilutions were made on serum samples from 5 colorectal cancer patients with DR-70 values in the range of 19.7 to 22.2 µg/mL with assay diluent buffer. For each CRC patient serum sample, a total of 9 diluted samples were tested. The following table lists the average % difference between the actual and the estimated DR-70 concentrations for each dilution as well as the average % recovery. The DR-70® FDP ELISA assay was linear from 1.5- 10 µg /mL with recoveries from 93 to 108%.

Table 4. DR70 Linearity

Estimated FDP Conc. ng/mL	Dilution Ratio	Highest Positive % Difference (n=5)	Lowest (Negative) % Difference (n=5)	Average % Difference	Average % Recovery
20	1	2.6	(14.5)	(4.4)	96
10	1/2	7.5	(7.4)	(1.0)	99
5	1/4	7.0	(2.6)	0.1	100
2.5	1/8	11.8	(21.2)	(7.0)	93
1.25	1/16	3.6	(14.5)	(5.7)	94
1.125	1/32	20.1	(5.8)	7.6	108
0.625	1/64	16.7	11.8	13.6	114

High dose hook effect (assessment of antigen excess)

No evidence of a hook effect was found up to a concentration of 200 µg/mL

Assay reportable range

Assay reportable range is from 0.063 to 10 μg/mL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):
There is no recognized reference standard for DR 70. Value assignment of the controls and calibrators was based on gravimetric method.

Stability
The DR-70® (FDP) Kit has an expiration date assignment of up to 18 months which is based on the component with the shortest dated stability data for the kit components. Real time stability studies have been conducted on each production lot of kits consisting from the initial date of QC up to the amount of months to the assigned kit expiration.

d. Detection limit
Analytical Sensitivity
The minimal detectable concentration (MDC) of DR-70® (FDP) is estimated to be 0.06 μg/mL. The MDC is defined as that concentration of DR-70® (FDP) corresponding to the absorbance that is two standard deviations from the mean rate of absorbance of 20 replicate determinations of a zero calibrator.

Functional Sensitivity
The functional sensitivity was determined by diluting the lowest non-zero calibrator serially, measuring the DR-70® (FDP) concentration and extrapolating to the point where the CV% = 20%. Functional sensitivity for the AMDL-ELISA DR-70® (FDP) was calculated as being between 0.052 and 0.063 μg/mL.

e. Analytical specificity and interference
Interference was defined, for purpose of this study, to be recovery > 10% of the known specimen mean concentration. Interferents (hemoglobin, bilirubin, triglyceride and heparin) were spiked into two patient serum pools with background man FDP concentrations at 1.07 and 2.2 μg/mL. Results showed that hemoglobin (up to 500 mg/dl), bilirubin (up to 30 mg/dl), triglyceride (up to 1000 mg/dl) and heparin (at concentrations of 500 U/ml) do not interfere with the assay.

In addition, the following pharmaceutical agents were tested at levels indicated and found not to cause analyte recovery > 10%: 5'-fluorouracil (Adrucil) 1.0 mg/mL; Acetaminophen 0.2 mg/mL; Adriamycin (Doxorubicin HCl) 0.10 mg/dL; Coumarin 1.4 mg/mL; Cyclophosphamide (Cytoxan) 0.25 mg/mL; Paclitaxel, 3.5×10^{-6} g/m^2; Amethopterin hydrate (Methotrexate) 4.5 mg/mL; Mitoxanntrone (Novatrone) 0.5 mg/mL; Folinic acid (Leucovorin) 1.10 mg/mL; Mitomycin C, 0.06 mg/mL and Cisplatin, 0.10 mg/mL.

f. Assay cut-off
A 15% increase from the previous visit was chosen as the threshold for significant % change for the determination of disease progression in the DR-70® (FDP) immunoassay based on the %total CV from the precision study. The total %CV was computed over all runs, days, and intra-assay for each

specimen analyzed and the highest CV values were observed for specimens with low DR 70 concentrations (0.21-0.42 µg/mL). Since over 80% of the DR 70 measurements in the cancer monitoring samples had concentrations ≥ 0.6 µg/mL, the sponsor used the average of the highest %CV obtained for samples with 1.31 (CV=7.85) and 4.11 (CV=7.14) µg/mL which was equal to 7.495%.

The δ (significant change in marker value) is equal to 1.96 times the %total CV. Using the value of 7.495%, the threshold for significant change was estimated to be 14.69% (7.495*1.96) rounded up to 15%. Thus if a later visit has a value that is greater than 15% higher than the previous value, it will be considered evidence of disease progression.

2. Comparison studies:
   a. *Method comparison with predicate device:*
      Not applicable since there is no predicate device.
   b. *Matrix comparison:*
      Not applicable, use of serum as specimen only.
3. Clinical studies:
   a. *Clinical Sensitivity and Clinical Specificity:*
      A clinical evaluation was performed to assess the DR 70 (FDP) assay for monitoring patients with colorectal cancer. Serial samples were taken from 112 colorectal cancer patients resulting in 445 paired observations (335 paired observations were post baseline samples). The sequential draws covered an average longitudinal period of at least nine months. The samples were retrospective banked samples that were collected blindly and without bias to include all patients with diagnosed colorectal cancer in the bank at the time of the collection. Inclusion and exclusion criteria for the samples were provided.

      The breakdown of the patient series is presented in Table 5. The average number of observations per patient is 4.0.

Table 5. Patient Observation Series

Number of Samples in Series	Number of Observation Pairs in Series	Total Number of Series with that Number of Pairs	Percent of the Total Samples	Cumulative Percent of Samples
2	1	1	0.9	0.9
3	2	38	33.9	34.8
4	3	48	42.9	77.7
5	4	18	16.1	93.8
6	5	3	2.7	96.5
7	6	3	2.7	99.2
8	7	1	0.9	100.0

Table 6 presents the stage of the disease at time of diagnosis for 111 of the 112 evaluable serial patients. One patient chart did not contain information related to the stage at time of diagnosis.

Table 6. Stage of Cancer at Time of Diagnosis

Stage at Diagnosis	Frequency	Percentage	Cumulative Percentage
0	1	0.9	0.9
I	4	3.6	4.5
II	18	16.2	20.7
III	39	35.1	55.9
IV	49	44.1	100.0
Total	111	100.0	

Table 7 demonstrates the relationship between stage at diagnosis and the presence of metastases. As the stage of the disease progressed, the percentage of patients with metastases increased.

Table 7. Distribution of Metastases by Stage at Diagnosis

	Known Metastases at time of Diagnosis:		
Stage	**Yes**	**No**	**Total**
0-I	0	5	5
	0.0%	100.0%	100.0%
II	3	15	18
	16.7%	83.3%	100.0%
III	29	10	39
	74.4%	25.6%	100.0%
IV	49	0	49
	100.0%	0.0%	100.0%
Total	81	30	111
	73.0%	27.0%	100.0%

Data analysis

Clinical disease progression was determined by the Subject's physician based on office procedures and clinical laboratory based analyses that were the standard of care during the time of the monitoring period. Progression of the DR-70 value was determined as a significant percentage change (15%) between the current and previous readings

The 335 paired observations from the post baseline sampling were evaluated in two ways. The initial analysis presents estimates directly from the data. This analysis is followed by a bootstrap sample for each patient by randomly sampling one visit from each sample and recording the sensitivity or specificity for that visit. Note that if there was a progression the sensitivity would be 1 if the DR-70 increased from the previous visit by 15% or more and 0 if it did not. If there were no progression at that visit, then there would be no sensitivity reported at that visit, but the specificity would be reported as 1 if the DR-70® (FDP) value was below a 15% increase for that visit and 0 otherwise. For the per-visit analysis, there were 135 visits for sensitivity and 198 visits for specificity.

A second analysis was done on a per-patient basis in which the number of progressions across all visits for a given patient was used to compute a patient level sensitivity by taking the number visits that DR-70 value increased by at least 15% among the number of visits in which there was a progression. Similarly, the number of visits at which DR-70 had a lower than 15% increase divided by the number of visits in which there was a non-progression allowed the computation of a per-patient specificity. If a patient had all progressions there would be no specificity for that patient and if a patient had all non-progressions, there would be no sensitivity for that patient. This resulted in a sample of 112 patients with at least one sensitivity, specificity, or both. This resulted in 70 estimates of per-patient sensitivity and 86 estimates of per-patient specificity.

Results of per-visit analysis

There were 10,000 bootstrap samples of 112 observations taken with replacement from the 334 paired observations. After each sample was taken, the following table was formed.

Table 8. Distribution of Progression by DR-70® (FDP) Value Increase from Previous Visit

		Disease Progression		
		No	**Yes**	**Total**
DR-70® (FDP)	**< 15%**	134	47	181
	≥15%	65	88	153
Total		199	135	334

The computed per-visit sensitivity from the 334 per-visit evaluations was 100*88/135= 65.19 with standard deviation (SD) 2.58, the specificity was 100*134/199= 67.34 with SD= 2.94, the sum of sensitivity and specificity was 132.53 with SD = 3.91, the PPV was 100*88/153= 57.52 with SD = 1.63, and the NPV was 100*134/181= 74.03 with SD = 2.44.

The results from the tabulations and per-visit bootstrap are shown in Table 9.

Table 9. Results of Tabulated and Five Repetitions of 2,000 Samples of 112 per-visit Observations of the Sensitivity, Specificity, the Sum of Sensitivity and Specificity, PPV, and NPV

Run	Measure	Median	Lower 5%	Lower 2.5%
From Data	Sensitivity	65.19	60.91	60.13
	Specificity	67.34	62.50	61.58
	Sensitivity + Specificity	132.53	126.10	124.87
	PPV	57.52	54.84	54.33
	NPV	74.03	70.02	69.25
Bootstrap 1	Sensitivity	65.85	55.81	54.17
	Specificity	66.20	59.09	57.63
	Sensitivity + Specificity	132.66	120.31	118.23
	PPV	58.33	50.91	49.23
	NPV	73.13	66.18	65.45
Bootstrap 2	Sensitivity	65.85	56.25	54.17
	Specificity	67.19	58.46	56.92
	Sensitivity + Specificity	132.92	120.75	118.72
	PPV	58.82	50.91	48.98
	NPV	73.21	66.18	64.91
Bootstrap 3	Sensitivity	65.91	56.10	54.00
	Specificity	67.16	58.73	56.92
	Sensitivity + Specificity	133.20	120.29	117.81
	PPV	58.93	49.15	48.94
	NPV	73.33	66.18	65.08
Bootstrap 4	Sensitivity	65.85	56.25	53.66
	Specificity	66.67	58.57	56.72
	Sensitivity + Specificity	132.96	119.73	116.99
	PPV	58.73	49.18	48.84
	NPV	73.13	66.00	64.52
Bootstrap 5	Sensitivity	65.96	56.25	54.90
	Specificity	67.16	58.73	57.38
	Sensitivity + Specificity	133.29	120.62	118.23
	PPV	59.02	50.88	49.09
	NPV	73.24	66.20	64.91

Using alpha = 0.05, the sum of sensitivity and specificity from this analysis clearly is statistically significantly above 100. The median sum is likely to be about 133 with the median sensitivity about 65 and the median specificity about 67. The lower two-sided 5% confidence bound is about 118. The median PPV and NPV are about 59 and 73, respectively, across the five samples. Note that these values are consistent with those computed from the per-visit values given above Table 9. The five repetitions of the sample of 2,000 demonstrate that the result is robust and consistent.

Results of per-patient analysis

For the per-patient analysis, the computed per-visit sensitivity from the 112 per-patient evaluations was 100*45.68/69 = 66.21, the specificity was 100*58.63/86= 68.18, the sum of sensitivity and specificity was 134.39, the

PPV was 100*51.83/97= 53.44, and the NPV was 100*71.67/103= 69.58.

The per-patient bootstrap per-patient results

The confidence intervals are obtained from the bootstrap evaluations below.

Table 10. Results of Five Repetitions of 2,000 Samples of 112 per-patient Observations of the Sensitivity, Specificity, the Sum of Sensitivity and Specificity, PPV, and NPV

Run	Measure	Median	Lower 5%	Lower 2.5%
Bootstrap 1	Sensitivity	66.12	58.78	57.11
	Specificity	68.20	62.58	61.46
	Sensitivity + Specificity	134.38	123.82	121.46
	PPV	53.30	45.88	44.55
	NPV	69.74	62.71	60.90
Bootstrap 2	Sensitivity	66.17	58.58	57.13
	Specificity	68.16	62.39	61.41
	Sensitivity + Specificity	134.26	123.85	122.17
	PPV	53.41	45.34	43.96
	NPV	69.50	62.75	61.37
Bootstrap 3	Sensitivity	66.13	58.59	57.27
	Specificity	68.20	62.29	61.23
	Sensitivity + Specificity	134.32	123.79	121.36
	PPV	53.37	45.71	43.89
	NPV	69.50	62.06	60.89
Bootstrap 4	Sensitivity	66.43	58.53	56.99
	Specificity	68.28	62.64	61.55
	Sensitivity + Specificity	134.69	123.87	121.17
	PPV	53.70	45.92	44.39
	NPV	69.55	62.71	61.33
Bootstrap 5	Sensitivity	66.42	59.00	57.92
	Specificity	68.29	62.82	61.64
	Sensitivity + Specificity	134.62	124.38	122.92
	PPV	53.41	45.75	44.15
	NPV	69.64	62.66	61.38

Using alpha = 0.05, the sum of sensitivity and specificity from this analysis is statistically significantly above 100. The median sum is likely to be about 134 with the median sensitivity about 66 and the median specificity about 68. The lower two-sided 5% confidence bound for the sum is about 121. The median PPV and NPV are about 53 and 69, respectively, across the five samples. Note that these values are consistent with those computed from the per-patient values given above Table 10. The five repetitions of the sample of 2,000 demonstrate that the result is robust and consistent.

The per-patient bootstrap results by cancer stage

The data are limited with respect to the stage of the cancer, but the analysis below presents the results of the estimates of sensitivity, specificity, sum, PPV, and NPV with confidence intervals computed with variances from the Emir et al (1998) method. The number of patients at each stage was 1 in

Stage 0, 4 in Stage 1, 18 in Stage 2, 39 in Stage 3, and 50 in Stage 4. For the purposes of this analysis, Stage 0-2 are combined in one analysis, and Stages 3 and 4 are analyzed separately.

The table of sensitivity, specificity, sum, PPV and NPV by cancer stage is given below. It should be noted that there were only 6 patients with 8 progressions in the Stage 0-2 group so the estimate of sensitivity will have large variability.

The per-patient bootstrap results by cancer stage are in the following table:

Table 11. Results of Sensitivity, Specificity, the Sum of Sensitivity and Specificity, PPV, and NPV by Cancer Stage

Stage	Measure	Median	Lower 5%	Lower 2.5%
0-2	Sensitivity	62.50	44.36	40.88
	Specificity	60.94	51.19	49.32
	Sensitivity + Specificity	123.44	102.84	98.90
	PPV	16.67	12.27	11.43
	NPV	90.70	78.58	76.26
3	Sensitivity	58.70	47.90	45.83
	Specificity	73.08	58.35	55.53
	Sensitivity + Specificity	131.77	113.51	110.02
	PPV	56.25	49.22	47.87
	NPV	75.00	63.60	61.40
4	Sensitivity	69.14	62.68	61.44
	Specificity	66.67	59.72	58.40
	Sensitivity + Specificity	135.80	126.32	124.51
	PPV	74.32	68.73	67.65
	NPV	60.32	54.75	53.69

Note that even among the stages with the lowest numbers of patients, the two-sided 5% lower confidence limit excludes 1 and the test retains its informative nature for Stage 3 and Stage 4. Predictably, as the prevalence increases across the stages, PPV increases and NPV decreases.

b. Other clinical supportive data (when a. is not applicable):

4. Clinical cut-off**:**
   For monitoring of disease status, fifteen percent (15%) or greater change from the previous visit for monitoring of disease progression.
5. Expected values/Reference range:
   The distribution of DR 70 concentrations determined in 1185 serum samples from normal subjects and patients with nonmalignant or malignant disease was evaluated. In this study, 84.5% of the normal subjects had DR-70 levels less than 1.5 µg/mL (Table 12).

Table 12. Distribution in Percent of Serum DR-70® (FDP) Values **

		Percent (%) 95% CI (lower-upper %)*			
Disease	**n**	**0-1.4 µg/ml**	**1.5-2.4 µg/ml**	**2.5-4.9µg/ml**	**≥ 5.0 µg/ml**
Normal	420	94.5 (91.9, 96.5)	5.0 (3.1, 7.5)	0.5 (0.1, 1.7)	0.0 (0.0, 0.9)
< 65 years	337	96.4 (93.9, 98.2)	3.3 (1.6, 5.8)	0.3 (0.0, 1.6)	0.0 (0.0, 1.1)
≥ 65 years	83	86.8 (77.5, 93.2)	12.1 (5.9, 21.0)	1.2 (0.0, 6.5)	0.0 (0.0, 4.4)
Benign	326	75.5 (70.4, 80.0)	6.8 (4.3, 10.0)	0.6 (0.1, 2.2)	17.2 (13.2, 21.7)
GU Disease	94	94.7 (88.0, 98.3)	4.3 (1.2, 10.5)	0.0 (0.0, 3.9)	1.1 (0.0, 5.8)
GI Disease	61	90.2 (79.8, 96.3)	3.3 (0.4, 11.4)	0.0 (0.0, 5.9)	6.6 (1.8, 16.0)
Pancreas	84	60.7 (49.5, 71.2)	15.5 (8.5, 25.0)	2.4 (0.3, 8.3)	21.4 (13.2, 31.7)
Heart Disease	87	58.6 (47.6, 69.1)	3.5 (0.7, 9.8)	0.0 (0.0, 4.2)	37.9 (27.7, 49.0)
Malignant	439	44.0 (39.3, 48.8)	24.2 (20.2, 28.4)	19.6 (16.0, 23.6)	12.3 (9.4, 15.7)
Colon	187	55.6 (48.2, 62.9)	21.4 (15.7, 28.0)	15.0 (10.2, 20.9)	8.0 (4.6, 12.9)
Lung	44	34.1 (20.5, 49.9)	38.6 (24.4, 54.5)	18.2 (8.2, 32.7)	9.1 (2.5, 21.7)
Liver	44	31.8 (18.6, 47.6)	27.3 (15.0, 42.8)	22.7 (11.5, 37.8)	18.2 (8.2, 32.7)
Breast	31	54.8 (36.0, 72.7)	25.8 (11.9, 44.6)	12.9 (3.6, 29.8)	6.5 (0.8, 21.4)
Ovarian	31	25.8 (11.9, 44.6)	6.5 (0.8, 21.4)	32.3 (16.7, 51.4)	35.5 (19.2, 54.6)
Cervical	28	50.0 (30.7, 69.4)	28.6 (13.2, 48.7)	7.1 (0.9, 23.5)	14.3 (4.0, 32.7)
Gall Bladder	19	42.1 (20.3, 66.5)	26.3 (9.2, 51.2)	31.6 (12.6, 56.6)	0.0 (0.0, 17.7)
Pancreas	28	25.0 (10.7, 44.9)	17.9 (6.1, 36.9)	35.7 (18.6, 55.9)	21.4 (8.3, 41.0)
Gastric/ Other	27	22.2 (8.6, 42.3)	33.3 (16.5, 54.0)	29.6 (13.8, 50.2)	14.8 (4.2, 33.7)

*Exact binomial confidence limits.

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