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

A. 510(k) Number:
k052889
B. Purpose for Submission:
New device.
C. Measurand:
CA 19-9
D. Type of Test:
Quantitative, EIA
E. Applicant:
Fujirebio Diagnostics, Inc.
F. Proprietary and Established Names:
VITROS Immunodiagnostics Products CA 19-9 Reagent Pack, VITROS
Immunodiagnostics Products CA 19-9 Calibrator, VITROS Immunodiagnostics
Products CA 19-9 Range Verifiers
G. Regulatory Information:
1. Regulation section:
21 CFR 866.6010, Tumor-associated antigen immunological test system
21 CFR 862.1150, Calibrator
21 CFR § 862.1660, Quality Control Material (Assayed and Unassayed)
2. Classification:
Class II, CA 19-9 assay and Calibrator
Class I, Quality control material
3. Product Code:
NIG, System, Test, Carbohydrate antigen (CA 19-9) for monitoring and
management of pancreatic cancer;
JIT, Calibrator, Secondary
JJX, Single (Specified) Analyte Controls (Assayed and Unassayed)
4. Panel:
Immunology (82)
Chemistry (75), Calibrator and Quality control material
H. Intended Use:
1. Intended use(s):
The VITROS Immunodiagnostics Products CA 19-9™ assay is for the *in vitro*
quantitative measurement of 1116-NS-19-9 defined antigen in human serum
and plasma (EDTA or heparin). The VITROS CA 19-9 assay is to be used to
aid in the management of patients diagnosed with cancers of the exocrine
pancreas. The VITROS CA 19-9 assay can be used to monitor disease status
in patients with confirmed pancreatic cancer who show measurable CA 19-9
values over the course of their disease. Serial CA 19-9 test results should be
used in conjunction with all other available clinical and laboratory data before
a medical decision is determined.

The VITROS CA 19-9™ Calibrator Kit is for *in vitro* use in the calibration of the VITROS Immunodiagnostic System for the quantitative measurement of 1116-NS-19-9 defined antigen in human serum and plasma (EDTA or heparin).

The VITROS CA 19-9™ Range Verifier Kit is for *in vitro* use in verifying the calibration range of the VITROS Immunodiagnostic System when used for the measurement of 1116-NS-19-9 defined antigen.

2. Indication(s) for use:
   Indicated for the serial measurement of CA 19-9 to aid in the management of patients diagnosed with cancers of the pancreas. Serial testing for patient CA 19-9 values is used in conjunction with other clinical methods in the management of pancreatic cancer patients.

3. Special condition for use statement(s):
   Patients must be Lewis blood group antigen positive. Patients known to be genotypically negative for Lewis blood group antigen are unable to produce the CA 19-9 antigen even in the presence of malignant tissue. Phenotyping for the presence of the Lewis blood group antigen may be insufficient to detect true Lewis antigen negative individuals. Even patients who are genotype positive for the Lewis antigen may produce varying levels of CA 19-9 as the result of gene dosage effect. The device is for prescription use only.

4. Special instrument Requirements:
   VITROS Immunodiagnostic ECi System (k962919)

I. Device Description:
The VITROS CA 19-9™ Reagent Kit consists of:
1. 100 streptavidin-coated wells
2. Conjugate reagent (HRP-mouse monoclonal anti-116-NS-19-9 defined antigen) in buffer with bovine serum albumin (BSA), bovine gamma globulin (BGG) and antimicrobial agent.
3. Biotinylated antibody reagent (biotin-mouse monoclonal anti-1116-NS-19-9 defined antigen) in buffer with BSA, BGG and antimicrobial agent.

The following reagents are required but not provided with the VITROS CA 19-9™ Reagent Kit:
The VITROS CA 19-9™ Calibrator Kit consists of Calibrators 1 (15 U/mL), 2 (60 U/mL) and 3 (700 U/mL) in buffer with BSA and antimicrobial agent, lot calibrator card, protocol card and bar code labels

The VITROS CA 19-9 Range Verifier Kit consists of Low (0 U/mL) and High (950 U/mL) verifiers in buffer with BSA and antimicrobial agent.

VITROS Immunodiagnostic Products Signal Reagent
VITROS Immunodiagnostic Products Universal Wash Reagent
Quality Control Materials e.g. VITROS Immunodiagnostic Products Oncology Controls
VITROS Immunodiagnostic Products High Sample Diluent B

VITROS Immunodiagnostic Products Reagent Pack Storage Box (optional) with desiccant

J. Substantial Equivalence Information:
    1. Predicate device name(s):
       Fujirebio Diagnostics CA 19-9™ RIA
    2. Predicate K number(s):
       k020566
    3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	VITROS CA 19-9™	Fujirebio CA 19-9 RIA
Intended Use	Quantitative analysis of CA 19-9 in human serum and plasma	Same
Indications for Use	As an aid in management of patients with cancers of the exocrine pancreas	Same
Antibody type and source	Monoclonal, mouse	Same

Differences		
Item	Device	Predicate
Methodology	Chemiluminescence Immunoassay	Solid phase RIA
Sample type	Serum and plasma (EDTA, lithium heparin and sodium heparin)	Serum or plasma (Citrate, heparin and EDTA)
Capture	Biotinylated mouse monoclonal anti-CA 19-9 (F(ab')2) captured by streptavidin on wells	Mouse monoclonal anti-CA 19-9 coated polystyrene beads
Conjugate antibody	Horseradish peroxidase-labeled mouse monoclonal anti-CA 19-9 (F(ab')2) conjugate	^{125}I conjugated monoclonal anti-CA 19-9 antibody
Substrate	Luminal derivative and peracid salt	None
Detection	Luminescence	Radioactivity
Calibrators	3 levels (1 = 15 U/mL, 2 = 60 U/mL and 3 = 700 U/mL)	6 levels (0-240 U/mL)
Controls	Not included Recommends use of VITROS Immunodiagnostic Products Oncology Controls every 24 hours	2 levels each run Low = 40 - 50 U/mL High = 80 - 90 U/mL
Range verifier	Provided separately	None
Instrument system	VITROS ECi System	Manual method
Measuring range	0-1000 U/mL	0-240 U/mL
Reaction time	≤ 1 hour	6 hours
Calibration frequency	Every 28 days	Every run
Sample size	35 μL	200 μL

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

Special guidance "Guidance Document for the Submission of Tumor Associated Antigen premarket Notifications (510(k)s) to FDA". CLSI guidelines include EP5-A (Evaluation of Precision Performance of Clinical Chemistry Devices), EP7-A (Interference Testing in Clinical Chemistry Devices), EP9-A2 (Method Comparison and Bias Estimation Using Patient Samples), EP6-P2 (Evaluation of the Linearity of Quantitative Analytical Methods – Proposed Guideline), C28-A2 (How to Define and Determine reference Intervals in the Clinical Laboratory) and EP14-A (Evaluation of Matrix Effects).

L. Test Principle:

The VITROS CA 19-9™ assay is a two-step immunometric assay. CA 19-9 antigen present in the sample reacts with a biotinylated mouse monoclonal anti-CA 19-9 antibody. The antigen-antibody complex is captured by streptavidin on the wells and unbound materials are removed by washing. After washing, HRP-labeled anti-CA 19-9 conjugate is added and binds to the CA 19-9 on the immobilized antigen/antibody complex. Unbound conjugate is removed by washing. When a reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent is added, the HRP in the bound conjugate catalyzes the oxidation of the luminal derivative and produces light. The electron transfer agent increases the level of light produced and prolongs the light emission. The light signals are read by the VITROS ECi Instrument System. The amount of HRP conjugate bound is directly proportional to the concentration of CA 19-9 in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   i. *Precision/Reproducibility:*
      Precision was evaluated according to CLSI EP5-A2. Three patient serum pools were tested in duplicate, two runs per day for 20 nonconsecutive days over 28 days on two instruments and two lots of CA 19-9 reagents and calibrators. Singleton determinations of the calibrators were performed on the first run of Day 1 (a) and again on the first run of the first day of each subsequent week (b). CA 19-9 values were determined by calibration curve established in (a) and (b). Results are summarized below.

Instrument	N	#Days	Mean Conc.	Within-run*		Within-calibration**		Within-lab***	
				SD (U/mL)	%CV	SD (U/mL)	%CV	SD (U/mL)	%CV
1	80	20	30.9	0.383	1.2	0.97	3.1	1.06	3.4
	80	20	98.0	0.884	0.9	2.55	2.6	2.54	2.6
	80	20	236	1.97	0.8	6.87	2.9	6.75	2.9
2	80	20	28.9	0.309	1.1	1.23	4.3	1.50	5.2
	80	20	90.2	1.18	1.3	3.50	3.9	4.41	4.9
	80	20	238	2.94	1.2	9.85	4.1	11.3	4.7

*Use duplicate determinations
** Use a single lot of reagents over a single calibration interval
*** Use a single lot of reagents calibrated weekly

      ii. *Linearity/assay reportable range:*

Linearity was evaluated according to CLIS EP6-P2. A low (7.38 U/mL CA 19-9) and a high (1091 U/mL CA 19-9) serum pool were mixed to give 7 pools of intermediate CA 19-9 concentrations. Ten singleton determinations of pool 1 and 9 and three singleton determinations of each of pool 2 to 8 were tested using two reagent and calibrator lots on one VITROS instrument. The concentrations of pool 2 to 8 were calculated using the following equation:

$$\frac{(L \times Conc.\ Pool\ 1) + (H \times Conc.\ Pool\ 9)}{10}$$

Where L = Ratio of Pool 1 used for blending, e.g. 9 for Pool 2
      H = Ratio of Pool 9 for blending, e.g. 1 for Pool 2

The means of Pools 1 and 9 were determined using 20 replicates from the combinations of Reagent/Calibrator. The means of Pools 2 to 8 were determined using the 6 replicates from both reagent/calibrator combinations and expressed as a percentage of the calculated concentrations. The percentage ranged from 96.9% to 102% with a mean of 99.3%. Linear regression analysis of the measured and calculated concentrations yielded a slope of 1.01, a y-intercept of -5.87 and $r^2 = 1$.

High sample dilution was assessed by assaying diluted series of 12 serum samples in singleton using two reagent and calibrator lots on two VITROS systems. The samples were diluted manually to 1/2, 1/5, 1/10, 1/15 and 1/20 with VITROS High Sample Diluent B. For samples with neat concentration above the assay range, the neat concentration was calculated from the first dilution. When compared to the neat sample, the overall mean percent recovery for all samples was 101% ranged from 97% to 108%.

Spike recovery – Ten normal human serum samples with known endogenous CA 19-9 leves were used. Aliquots of each sample were spiked with a different concentration of CA 19-9 (120.8, 249.47, 528.3 and 832.0 U/mL). Each sample was assayed in duplicate. The mean percent recovery across all concentrations and all samples was 93.1% (ranged from 90.4% to 96.8%) and met the acceptance criterion of 100 ± 15%.

The assay measuring range is from 0 U/mL to 1000 U/mL.

iii.   *Traceability, Stability, Expected values (controls, calibrators, or methods):*
There is no known reference standard for CA 19-9. The VITROS CA 19-9™ reference calibrators were standardized against the Fujirebio Diagnostics, Inc. CA 19-9 reference preparation. The VITROS CA 19-9™ reference calibrators are manufactured volumetrically and assayed using the Fujirebio Diagnostics Inc. CA 19-9™ RIA assay. The values were validated by a panel of patient serum samples measured by both

VITROS and Fujirebio Diagnostics Inc. CA 19-9™ assays. The VITROS reference calibrators are used for manufacture of the calibrator kits.

iv. *Detection limit (functional sensitivity):*
The minimal detectable dose (MDD) was determined by testing two lots of VITROS CA 19-9™ Calibrator Matrix (0 U/mL) and each of 5 serum samples with CA 19-9 values < 5 U/mL in replicates of 10 on three instruments using two lots of calibrators and two lots of VITROS CA 19-9™ Reagents. The LOD was defined as the limit of the blank (LOB) plus one tailed-95% confidence range for a low sample, i.e. 1.645 (SD of low sample). Two lots of the low range verifier were used to determine LOB. Since the instrument only reports positive results, results were pooled and the rank order method was used to determine the 95th percentile for the assay and LOB was determined to be 1.05 U/mL. Five samples were used to determine the sample SD. Samples with average values below zero were excluded from analysis. The pooled SD of the remaining samples was 0.277 U/mL. The LOD is equal to (LOB + 1.645SD$_{sample}$) which is 1.42 U/mL.

v. *Analytical specificity:*
Endogenous substances - Interference was determined by spiking a known amount of an interfering substance into aliquots of five serum samples supplemented with CA 19-9. Interfering substances tested included hemoglobin (150, 300 and 600 mg/dL), bilirubin (22 mg/dL), triglycerides (3000 mg/dL), biotin (10 ng/mL) and total protein (10 g/dL). Spiked and non-spiked samples were tested in duplicate and percent recoveries were calculated. Except for hemoglobin which is a known interferent, the percent mean recoveries for the other substances ranged from 97.2% for total protein to 100.2% for bilirubin at the levels tested. The average recoveries for hemoglobin levels 150, 300 and 600 mg/mL were 114.4%, 133.2% and 156.4% respectively. A warning is included in the package insert under Limitations of the Procedure.

Chemotherapeutic substances – Interference was determined by spiking the following pharmaceutical compounds into aliquots of five CA 19-9 supplemented serum samples and assayed: Leucovorin/Folinic Acid (11.4 mg/dL), Gemzar/Gemcitabine HCl (38.2 mg/dL), Streptozotocin/Zanosar (28 mg/dL), Doxorubicin (40 μg/mL). Cyclophosphamide/Cytoxan (37.5 mg/dL), Cisplatin-Dichloride (5.7 mg/dL), 5-Flourouracil/Adrucil (39 mg/dL), Methotrexate/Amethopterin-Hydrate (91 mg/dL), Tamoxifen (2.28 μg/dL), Cytarabine (3 mg/dL) and Paclitaxel/Taxol (6.7 mg/dL). Spiked and non-spiked samples were tested in replicates and percent recoveries were calculated. At the concentrations tested, the percent mean recoveries ranged from 96.8% to 105.5%.

Human anti-mouse antibody (HAMA) - To assess interference due to HAMA, five HAMA positive samples and one normal sample were studied. Each sample was split into three aliquots. One aliquot was

spiked with CA 19-9 antigen to achieve 35 U/mL while the second aliquot was spiked with the same volume of antigen to achieve 250 U/mL. The third aliquot was spiked with an equivalent volume of antigen free matrix and served as the control. All aliquots were run in duplicate in the same run. Percent recoveries were calculated and for the HAMA samples with 35 U/mL CA 19-9, the % recovery ranged from 88.9% to 100% (mean = 96.7%) and for samples with 250 U/mL CA 19-9, the % recovery ranged from 92.1% to 100.6% (mean = 97.5%). The following table summarizes the results.

Sample	HAMA (ng/mL)	CA 19-9			% Recovery	
		Neat	35 U/mL	250 U/mL	35 U/mL	250 U/mL
1	14.5	16.3	53.4	287	100	100.5
2	55.0	4.0	40.1	275	97.3	100.6
3	115	7.3	43.4	268	97.3	96.8
4	215	8.8	45.9	272	100	97.7
5	340	0	33.0	248	88.9	92.1
Normal	0	12.7	49.8	282		
Average (normal excluded)					96.7	97.5

Rheumatoid factor (RF) - To assess interference due to RF, five RF positive samples and one normal sample were tested. Each sample was split into three aliquots. One aliquot was spiked with CA 19-9 antigen to achieve 35 U/mL while the second aliquot was spiked with the same volume of antigen to achieve 250 U/mL. The third aliquot was spiked with an equivalent volume of antigen free matrix and served the control. All aliquots were run in duplicate in the same run. Percent recoveries were calculated and recoveries for samples with 35 U/mL CA 19-9 ranged from 84.6% to 98.4% (mean = 93.4%) and for samples with 250 U/mL CA 19-9, % recovery ranged from 90.9% to 98.3% (mean = 95.6%).

Sample	RF (ng/mL)	CA 19-9			% Recovery	
		Neat	35 U/mL	250 U/mL	35 U/mL	250 U/mL
1	20.9	68.4	103.0	333	93.3	98.3
2	84.0	0.1	31.5	245	84.6	90.9
3	159	22.9	58.6	287	96.2	98.1
4	323	3.0	38.0	262	94.3	96.2
5	593	27.0	63.5	286	98.4	96.2
Normal	0	12.7	49.8	282		
Average (normal excluded)					93.4	95.6

Cross-reactivity
No data provided.

vi. *Assay cut-off:*
See Expected Value.
2. Comparison studies:
i. *Method comparison with predicate device:*
Two hundred twenty-five serum samples were tested on the VITROS CA 19-9™ assay and the Fujirebio CA 19-9™ RIA Assay. All samples with

values outside the dynamic range of the Fujirebio assay were diluted per package inserts. Twenty-four samples were excluded from analysis because the CA 19-9 values were below the LOD of the VITROS (23) and/or Fujirebio assay (10). Twenty-five samples with CA 19-9 values above 1000 U/mL were also excluded. The remaining 176 samples were analyzed by Passing-Bablok linear regression analysis. The CA 19-9 concentrations of the specimen as determined by the Fujirebio CA 19-9™ RIA ranged from 2.36 to 892 U/mL as compared to 1.7 to 653 U/mL on the VITROS assay. The Passing-Bablok linear regression analysis yielded a slope of 0.83 (95% CI 0.80, 0.88) and y-axis intercept of -0.40 U/mL (95% CI -1.3, -0.27) with a Spearman Correlation coefficient of 0.93.

In addition to regression analysis, samples were also evaluated to the percent agreement with the predicate device using 37 U/mL as the cut-off (see table below):

		CA 19-9 RIA		
		≤ 37 U/mL	> 37 U/mL	Total
VITROS CA 19-9	≤ 37 U/mL	132	14	146
	> 37 U/mL	0	79	79
	Total	132	93	225

Percent positive agreement   100% (132/132)
Percent negative agreement   84.9% (79/93)
Percent total agreement   93.8% (211/225) (95% CI: 89.8%, 96.6%)

ii.   *Matrix comparison:*
      Matched human serum and plasma samples were collected in the following tube types: serum clot, serum separator tube (SST), EDTA, lithium heparin and sodium heparin. Twenty-six sample sets were assayed unchanged. Sample sets from 24 subjects were subdivided into 4 groups and each group was spiked with different concentrations of CA 19-9 (final concentrations of 50, 100, 200 and 650 U/mL). All samples were tested in duplicate and within 36 hours of sample draw. Results of the average recovery for each anticoagulant are summarized below.

CA 19-9 (U/mL)	Average % Recovery			
	SST	EDTA	Sodium Heparin	Lithium Heparin
50	105.1	103.4	101.1	102.1
100	99.7	95.4	97.1	95.7
200	100.4	94.7	96.6	95.4
650	100.9	98	97.5	98.8
Total % and (SD)	100.7 (5.1)	97.9 (8.2)	96.9 (5.5)	96.9 (5.2)
CA 19-9 (U/mL)	Average U/mL Recovery and (SD)			
1.1 to 19.5	0.8 (2.4)	0.1 (1.7)	0 (1.6)	0.3 (1.5)
20 to 46	97.5	97.9	92.3	92.5

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):*
    Serial Monitoring Analysis
    Two hundred and sixty one serum samples from 74 patients with confirmed pancreatic cancer collected and banked at two US clinical sites were analyzed. The average number of sample pairs per patient was 3.5 (see table below)

Number in Series	Number of Observation Pairs	Frequency	Percent
3	2	36	48.6
4	3	37	50.0
5	4	1	1.4

The average age of the patients at the time of diagnosis was 61.8 years ranging from 41 to 85 years. Fifty-five percent were males and forty-five percent females. Eighty percent of the patients were Caucasians, the remaining 20% consisted of African-Americans (11%), Hispanics (8%) and Asians (1%). Only 9% of the patients were current smokers, 51% were past smokers and 38% nonsmokers (smoking status of one patient was unknown). At the time of diagnosis, 30% of the patients had diabetes and 27% had other medical conditions. Of the diabetic patient subset, 64% were males.

Seventy of the 74 patients had disease stage information: 3 Stage I, 5 Stage II, 31 Stage III, and 31 Stage IV. Ninety-five percent of the pancreatic tumors were adenocarcinomas with 65% involving the head of the pancreas. In addition, histology stratification showed that 13.51% were well differentiated, 22.97% moderately differentiated, 5.41% poor to moderately differentiated, 12.16% poorly differentiated and 45.95% as other.

Changes in CA 19-9 concentrations and changes in disease state were analyzed on a per-visit basis. A significant change in CA 19-9 was defined as greater than 12.5% (2.5 times the total precision %CV). The following tables show the association between CA 19-9 concentrations and disease status for the 187 evaluable observation pairs. The 95% confidence intervals for the concordance statistics were based on General Estimable Equations and calculated using the GENMOD procedure of SAS.

	Change in Disease State		
Changes in CA 19-9	Progression	No Progression	Total
≥ 12.5%	15	58	73
< 12.5%	18	96	114
Total	33	154	187

Positive concordance = 0.455 (15/33) (95% CI: 0.284, 0.637)
Negative concordance = 0.623 (96/154) (95% CI: 0.544, 0.696)
Total concordance = 0.594 (111/187) (95% CI: 0.519, 0.664)

Fujirebio RIA	Change in Disease State		
Changes in CA 19-9	Progression	No Progression	Total
≥ 20%	15	51	66
< 20%	18	103	121
Total	33	154	187

Positive concordance = 0.455 (15/33) (95% CI: 0.284, 0.637)
Negative concordance = 0.669 (103/154) (95% CI: 0.585, 0.743)
Total concordance = 0.631 (118/187) (95% CI: 0.554, 0.702)

Serial monitoring results were also analyzed on a per-patient basis as shown below. Concordances and 95% CI were determined. Confidence intervals for these estimates were determined using binomial distribution.

	Change in Disease State		
Changes in CA 19-9	Progression	No Progression	Total
≥ 12.5%	15	18	33
< 12.5%	7	34	41
Total	22	52	74

Positive concordance = 0.682 (15/22) (95% CI: 0.451, 0.861)
Negative concordance = 0.654 (34/52) (95% CI: 0.509, 0.780)
Total concordance = 0.662 (49/74) (95% CI: 0.543, 0.768)

Fujirebio RIA	Change in Disease State		
Changes in CA 19-9	Progression	No Progression	Total
≥ 20%	14	18	32
< 20%	8	34	42
Total	22	52	74

Positive concordance = 0.636 (14/22) (95% CI: 0.407, 0.828)
Negative concordance = 0.654 (34/52) (95% CI: 0.509, 0.780)
Total concordance = 0.649 (48/74) (95% CI: 0.529, 0.756)

4. Clinical cut-off:
   Not applicable.
5. Expected values/Reference range:
   The normal reference range was established by testing serum samples from 200 subjects (100 males and 100 females). No other demographic information was provided. Samples were assayed in singleton. The mean CA 19-9 concentration was 11.53 U/mL (SD = 11.67 U/mL) and median of 7.955 U/mL. A cumulative distribution was established and the 99th percentile was determined to be 62.71 U/mL, the 97.5[th] percentile was 37.3 U/mL and the 95th percentile was 31.58 U/mL. The table below shows the distribution of CA 19-9 results.

# subjects	CA 19-9 Values		
	≤37.0 U/mL	37.1-70 U/mL	> 70 U/mL
200	194	6	0

In addition to the normal cohort, 417 serum samples from 187 patients with benign conditions and 230 from patients with malignant diseases were tested. The following table summarizes the sample distribution, diseases/conditions, distribution and median CA 19-9 results.

Cohort	# Subjects	Distribution of CA 19-9 Values			Median & (Mean) CA 19-9 (U/mL)
		≤ 37.0 U/mL	37.1-70 U/mL	≥ 70 U/mL	
Nonmalignant Disease					
Colorectal	30	27	2	1	7.8 (15.9)
Cirrhosis	67	59	2	6	12.2 (34.9)
Non-GI	40	36	4	0	7.38 (13.7)
H. Pylori	50	46	4	0	6.78 (12.6)
Malignant Disease					
Pancreatic	50	15	2	33	231
Colorectal	100	49	8	43	41.5
Somach	30	19	1	10	13.0
Lung	50	31	7	12	25.6

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.