510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k050231

B. Purpose for Submission:
This is a new device.

C. Measurand:
CA 19-9

D. Type of Test:
Quantitative, automated, two step sandwich, electrochemiluminescence immunoassay

E. Applicant:
Roche Diagnostics Corp.

F. Proprietary and Established Names:
Elecsys CA 19-9 Immunoassay
Elecsys CA 19-9 CalSet

G. Regulatory Information:
1. Regulation section:
   21 CFR 866.6010, Tumor-associated antigen immunological test system
   21 CFR 862.1150, Calibrator
2. Classification:
   Class II
3. Product Code:
   NIG, System, Test, Carbohydrate antigen (CA 19-9) for monitoring and management of pancreatic cancer;
   JIT, Calibrator, Secondary
4. Panel:
   Immunology (82)

H. Intended Use:
1. Intended use(s):
   The Elecsys CA 19-9 Immunoassay is an immunoassay for the in vitro quantitative determination of CA 19-9 tumor associated antigen in human serum and plasma. The assay is indicated for the serial measurement of CA 19-9 to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The test is useful as an aid in the monitoring of disease status in those patients having confirmed pancreatic cancer who have levels of CA 19-9 at some point in their disease process exceeding the median concentration determined for the apparently healthy cohort. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the

Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

The Elecsys CA 19-9 CalSet is used for calibrating the quantitative Elecsys CA 19-9 assay on the Elecsys immunoassay systems.

2. Indication(s) for use:
   As an aid in the management of patients diagnosed with cancers of the exocrine pancreas and in monitoring of disease status in those patients having confirmed pancreatic cancer who have levels of CA 19-9 at some point in their disease process exceeding the median concentration determined for the apparently healthy cohort.

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:
   Use with Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers. These systems were 510(k) cleared under k961481.

I. Device Description:
The Elecsys CA 19-9 Immunoassay kit consists of 1 bottle each of M. streptavidin-coated microparticles, biotinylated monoclonal anti-CA 19-9 antibody (Ab) in phosphate buffer (R1) and ruthenium complex labeled monoclonal anti-CA 19-9 Ab in phosphate buffer (R2). Reagents are assembled into a ready-for-use unit. All reagents contain preservative.

The Elecsys CA 19-9 CalSet consists of two levels of human CA 19-9 (approximately 20 U/mL and 200 U/mL) in lyophilized human serum with preservative. Included with the calibrators are barcode card, barcode sheet, 4 empty labeled snap-cap bottles and 12 bottle labels. Each reagent is reconstituted with 1.0 mL of distilled water

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
	Elecsys CA 19-9	**Fujirebio CA 19-9 RIA**

Similarities		
Item	Device	Predicate
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	Electrochemiluminescent enzyme immunoassay	Radioimmunoassay
Solid Phase	Streptavidin-coated microparticles	CA 19-9 antibody-coated polystyrene beads
Sample type	Serum and plasma (K_3 EDTA, lithium heparin, NH_4-heparin and sodium heparin)	Serum
Conjugate Antibody	Biotinylated anti-CA 19-9 and ruthenium labeled anti-CA 19-9	[125]I conjugated monoclonal antibody
Calibrators	2 levels ($\approx$ 20 and 250 U/mL)	6 levels (0-600 U/mL)
Controls	2 levels (PreciControl Tumor Marker) 20 and 100 U/mL	3 levels Low = 30 U/mL Medium = 80 U/mL High = 200 U/mL
Instrument System	Elecsys 1010, 2010 and MODULAR ANALYTICS E170	Manual method or semi-automated with commercially available rinsing/aspiration systems
Measuring range	0.60-1000 U/mL	0.9-240 U/mL

K. Standard/Guidance Document Referenced (if applicable):
None referenced.

L. Test Principle:
The Elecsys CA 19-9 Assay is a two-step sandwich immunoassay. A sample is incubated with a biotinylated monoclonal CA 19-9 antibody and a ruthenium complex labeled monoclonal CA 19-9 antibody. If CA 19-9 is present in the sample, it will bind to both antibodies to form a sandwich complex. After addition of the streptavidin-coated microparticles, the complex will bind to the microparticles as the result of interaction of biotin and streptavidine. The reaction mixture is aspirated into a measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are removed with system buffer. Application

of a voltage to the electrode induces chemiluminescent emission which is measured by a photomultiplier. Results are determined using a calibration curve generated by a 2 point calibration and a master curve provided with the reagent bar code.

M. Performance Characteristics (if/when applicable):
  1. <u>Analytical performance:</u>
     i. *Precision/Reproducibility:*
        Precision was evaluated on Elecsys 2010 Immunoassay Analyzer by testing 6 replicates each of two controls (CA 19-9 concentrations of 19.2 and 60.6 U/mL) and 3 patient samples (CA 19-9 concentrations of 11.1, 46.6 and 185.4 U/mL) per day for 10 days. The following table summarized the results of the with-in run and total precision.

Sample	Mean (U/mL)	Within-run SD (U/mL)	Within-run %CV	Total SD (U/mL)	Total %CV
Control 1	19.2	0.85	4.4	0.93	4.8
Control 2	60.6	1.75	2.9	2.28	3.8
Serum 1	11.1	0.40	3.6	0.45	4.1
Serum 2	46.6	46.6	3.3	1.75	3.8
Serum 3	185.4	5.31	2.9	5.42	2.9

Additional data were provided for five human serum samples with CA 19-9 concentrations of 36.81, 159.79, 307.47, 644.61 and 919.78 U/mL. These samples were tested in duplicate on four Elecsys 2010 instruments with two series per instrument. The total %CV across all instruments ranged from 1.6% to 4.4%. Lot-to-lot comparison was performed on 5 lots with 5 control samples with the following CA 19-9 concentrations: 12.6, 16.7, 20.8, 71.7 and 196 U/mL. The %CV ranged from 1.7% to 3.5%.

     ii. *Linearity/assay reportable range:*
        Linearity was evaluated by assaying 3 serum samples containing varying concentrations of CA 19-9 (1138.6, 866.7 and 1400.4 U/mL). Each sample was serially diluted with sample diluent to 14 dilutions, from undiluted to samples containing 0.6% serum. The observed results were compared to the expected results and the percent recovery was calculated. The percent recoveries ranged from 85.4% to 104.5%.

        The assay measuring range is from 0.6 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 Elecsys CA 19-9 assay was standardized against the Enzymun CA 19-9 manufactured by Boehringer Mannheim Immunodiagnostics. The master calibrators and secondary calibrators are prepared using human CA 19-9 spiked into human serum matrix. Value assignment is based on the Enzymun CA 19-

9. The CalSets are assayed and compared to these standard preparations and values are assigned. This assignment process utilizes four E170, four Elecsys 2010 and four Elecsys 1010 analyzers. Two series of analyses are performed on each instrument. Two-fold determinations are made for each series.

PreciControl Tumor Marker is the control material for the Elecsys CA 19-9. PreciControl Tumor Marker was originally cleared under k972235. A special 510(k) will be submitted for the PreciControl Tumor Marker to obtain clearance for the additional analyte. CA 19-9 analyte is a constituent of the already cleared PreciControl Tumor Marker but remains silent in the product labeling as no Elecsys CA 19-9 immunoassay is yet available in the US.

iv. *Detection limit (functional sensitivity):*
The lower detection limit (LDL) was determined on the Elecsys 2010 Immunoassay Analyzer by calculating the concentration of CA 19-9 that would give a response equal to the mean of the CA 19-9 Master Low calibrator plus two standard deviations (SD). Three runs of 21 replicates of the Low calibrator were performed. The results were expressed in counts and then converted to U/mL using the slope and intercept of the standard curve. The mean counts + 2SD were 1486, 1553 and 1530 which were equivalent to 0.13 U/mL, 0.28 U/mL and 0.1 U/mL. The mean LDL claim is <0.6 U/mL.

v. *Analytical specificity:*
Endogenous substances - Interference was determined by using natural and spiked samples and assayed on the Elecsys 2010. Interfering substances tested include hemoglobin, biotin, intralipid, bilirubin and rheumatoid factor. No significant interference was observed for bilirubin <66 mg/dL, hemoglobin <2.2 g/dL, intralipid <1500 mg/dL, biotin <100 ng/mL and rheumatoid factor ≤1500 IU/mL.

Pharmaceutical compounds – Interference was determined by spiking the following pharmaceutical compounds into natural patient samples and assayed on Elecsys 2010 Immunoassay Analyzer: acetylcystein (150 mg/L), ampicillin (1000 mg/L), ascorbic acid (300 mg/L), ca-dobesilate (200 mg/L), cyclosporine (5 mg/L), cefoxitin (2500 mg/L), levodopa (20 mg/L), methyldopa (20 mg/L), metronidazole (200 mg/L), phenylbutazone (400 mg/L), acetysalicylic acid (1000 mg/L), rifampicin (60 mg/L), intralipid (10000 mg/L), acetaminophen (200 mg/L), ibuprofen (500 mg/L), theophyllin (100 mg/L), doxorubicin (75 mg/L). cyclophosphamid (1000 mg/L), cisplatin (225 mg/L), 5-flourouracil (500 mg/L), methothrexat (50 mg/L), tamoxifen (50 mg/L), mitomycin (25 mg/L), carboplatin (1000 mg/L), etoposid (400 mg/L), flutamid (100 mg/L) and taxol (5.5 mg/L). No interference was observed at the concentrations tested.

Human anti-mouse antibody (HAMA) - To assess interference due to HAMA, a sample with known amount of CA 19-9 (93.5 U/mL) was

spiked into serial dilutions of a sample with known HAMA concentration (45 µg/mL) and known intrinsic concentration of CA 19-9 of 11.95 U/mL. At all dilutions, recovery of CA 19-9 was in the range of 100 to 102%. The same samples were likewise tested with reagents without the HAMA inhibiting proteins and falsely elevated results corresponding to 921.7 U/mL of CA 19-9 was obtained. Another HAMA positive sample (207 U/mL) tested also gave falsely elevated CA 19-9 concentrations of 747.8 U/mL as compared to 18.5 U/mL of the same sample with HAMA inhibiting reagents.

Cross-reactivity - Other tumor antigens (TM) was assessed for potential cross-reactivity by testing CA 19-9 positive serum samples that were spiked with known concentrations of TM. The samples were assayed on the Elecsys 2010 and results were summarized below.

Unspiked serum CA 19-9 (U/mL)	TM Added	TM Concentration	Measured CA 19-9 (U/mL)	Recovery (%)
452.9	PSA	100 ng/mL	448.5	99
452.9	AFP	300 ng/mL	441.0	97
386.5	CEA	1 µg/mL	422.3	109
386.5	CA 15-3	100 U/mL	415.6	108
386.5	CA 125	1000 U/mL	408.5	106

   vi.   *Assay cut-off:*
         See Expected Value.
5. Comparison studies:
   i.   *Method comparison with predicate device:*
        One thousand three hundred and fifty three serum samples were tested on the Elecsys CA 19-9 assay and the Fujirebio CA 19-9 Assay. These samples were collected from male and female subjects who were either normal, with benign or malignant diseases. The CA 19-9 concentrations of the samples ranged from 0 to 174,340 U/mL using the predicate device. The assays were performed in singlicate for the new device and duplicate for the predicate device. The results were analyzed by Passing-Bablok linear regression and results are shown below. The bias observed could likely reflect differences in technology.

Passing-Bablok Linear Regression Analysis for Elecsys (y) versus Fujirebio (x) Data for Various CA 19-9 Populations

Analysis	Slope (95%CI)	Intercept (95% CI)	Correlation Coeffient (Pearson r)	Number (X Range, U/mL)	md(95)
Apparently Healthy	0.95 (0.90 to 1.01)	0.80 (0.45 to 1.05)	0.7599	403 (0 to 64)	11.8
Benign	0.84 (0.79 to 0.89)	0.97 (0.52 to 1.40)	0.8648	456 (0 to 161)	12.9
Malignant <1,000 U/mL	0.76 (0.72 to 0.871)	2.19 (1.59 to 2.85)	0.8432	449 (0 to 979)	130
Malignant <10,000 U/mL	0.70 (0.65 to 0.74)	2.86 (2.19 to 3.54)	0.9182	477 (0 to 6,938)	292
Cumulative <1,000 U/mL	0.84 (0.81 to 0.87)	1.30 (0.97 to 1.57)	0.8576	1308* (0 to 979)	30.7
Cumulative <10,000 U/mL	0.81 (0.78 to 0.84)	1.51 (1.20 to 1.78)	0.9222	1336** (0 to 6,938)	79.4

* 45 malignant specimens had values > 1,000 U/mL
** 17 malignant specimens had values >10,000 U/mL

Results were also analyzed for samples that were within the assay range of the predicate device (0-240 U/mL). The cumulative slope was 0.88 (95% CI: 0.85, 0.91) and intercept was 1.00 (95% CI: 0.74, 1.32). The slope and intercept for the malignant samples <240 U/mL were 0.87 (95% CI: 0.81, 0.93) and 1.44 (95% CI: 0.82, 2.04) respectively.

ii.   *Matrix comparison:*
Plasma samples collected in lithium heparin, sodium heparin, NH_4 heparin and K3 EDTA were compared to matched-serum samples and analyzed using the Elecsys CA 19-9 assay. All samples had CA 19-9 concentrations < 31 U/mL. The number of paired samples tested varied with the anti-coagulant. Results were analyzed by Least Squares and Passing-Bablok regression analyses and are summarized below.

	Sodium & Lithium Heparin		NH_4 Heparin		EDTA (Study 1 & 2*)	
	Passing Bablock	Least Squares	Passing Bablock	Least Squares	Passing Bablock	Least Squares
N	20		14		20 (14)	
Range	2.5-30.3		5.5-20.8		2.64-30.0 (5.5-20.8)	
Slope	0.98	0.98	0.98	0.96	0.94 (0.94)	0.94 (0.93)
Y-Intercept	0.22	0.14	0.24	0.48	-0.2 (0.11)	-0,2 (0.21)
r	1.00	1.00	0.912	0.997	0.98 (0.956)	1.0 (0.994)
SEE	0.30	0.30	0.22	0.27	0.17 (0.28)	0.23 (0.33)

*EDTA Study 2 in ()

Additional study was performed with 20 paired serum and plasma samples for each anticoagulant with CA 19-9 concentration ranged from 23.8 U/mL to 934.5 U/mL. Results are tabulated below:

Passing Bablock	Sodium Heparin	Lithium Heparin	NH$_4$ Heparin	EDTA
Slope (95% CI)	1.00 (0.99-1.02)	1.00 (0.98-1.02)	0.99 (0.96-1.03)	0.99 (0.97-1.01)
Y-Intercept (95% CI)	-2.86 (-7.31-5.47)	-1.68 (-5.37-5.15)	-0.30 (-7.04-12.14)	2.85 (-2.47-10.60)
r	0.99	0.99	0.99	0.99

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
      Three hundred ninety-one serum samples from 95 patients with confirmed pancreatic cancer were prospectively collected and banked at two US clinical sites. Samples from six patients were excluded from the statistical analysis. Four patients ((#003, #007, #014 and #026) were excluded because all samples had zero CA 19-9 results on the predicate and test device. These subjects were considered Lewis blood group non-secretors. Two patients (#004 and #048) were excluded because they did not meet the inclusion criteria. Patient #004 had primary duodenal cancer with pancreatic involvement and Patient #048 was diagnosed with prostate cancer in addition to the primary pancreatic cancer during the study. Of the remaining 89 patients, 74 were Caucasians, 2 African Americans, 9 Hispanics, 1 Asian and 3 others. The mean and median age of the cohort was 62.4y (ranged from 36y to 83.3y) and 63y respectively. The female subjects had a mean age of 64.6y (36y to 83.3y) and median age of 67.5y whereas the mean age of the male subjects was 60.4y (43.8y to 78.4y) and median age 60.5y.

      There were 363 samples with an average number of 4.08 observations per patient (ranged from 1 to 13 sample pairs). The breakdown of the patient series is summarized below.

# Samples in Series	#Observation Pairs	Frequency	%
2	1	14	15.7
3	2	27	30.3
4	3	17	19.1
5	4	19	21.3
6	5	5	5.6
7	6	2	2.2
8	7	3	3.4
10	9	1	1.1
13	12	1	1.1

      At the time of diagnosis, 87 of the 89 patients had stage information: 14.9% were Stage I, 26.4% Stage II, 24.1% Stage III and 34.5% stage IV. Metastases were detected in 23.1% of Stage I patients, 47.8% Stage II, 57.1% Stage III and 80% Stage IV. The average (± SD) length of time in the study was 250 (± 338.8) days ranging from 14 days to 2013 days.

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 15% for both new and predicate devices. The following tables show the association between CA 19-9 concentrations and disease status for the 274 evaluable observation pairs. Concordance results for test and predicate devices are given in tables below. The data in the tables represent "panel" data. Since each subject brings a unique set of visit pairs, the Genmod Procedure of SAS was used to obtain estimates of concordance.

Elecsys	Change in Disease State		
Changes in CA 19-9	Progression	No Progression	Total
Increase >15%	54	65	119
No Significant Increase	33	122	155
Total	87	187	274

Positive concordance = 0.621 (54/87) (95% CI: 0.493, 0.733)
Negative concordance = 0.652 (122/187) (95% CI: 0.588, 0.711)
Total concordance = 0.642 (176/274) (95% CI: 0.584, 0.696)

Predicate	Change in Disease State		
Changes in CA 19-9	Progression	No Progression	Total
Increase >15%	51	63	114
No Significant Increase	36	124	160
Total	87	187	274

Positive concordance = 0.586 (51/87) (95% CI: 0.478, 0.686)
Negative concordance = 0.663 (124/187) (95% CI: 0.601, 0.719)
Total concordance = 0.639 (175/274) (95% CI: 0.586, 0.688)

The 3x3 tables below depict the distribution of clinical change by marker change for the test device and the predicate device.

	Clinical Status			
Elecsys	Response	No Change	Progression	Total
<-15%	21 (7.7%)	40 (14.6%)	20 (7.3%)	81 (29.6%)
-15% to 15%	15 (5.5%)	46 (16.8%)	13 (4.7%)	74 (27.0%)
>15%	14 (5.1%)	51 (18.6%)	54 (19.7%)	119 (43.4%)
Total	50	137	87	274

| Predicate | Clinical Status | | | |
	Response	No Change	Progression	Total
< -15%	29 (10.6%)	41 (15.0%)	20 (7.3%)	90 (32.8%)
-15% to 15%	9 (3.3%)	45 (16.4%)	16 (5.8%)	70 (25.6%)
>15%	12 (4.4%)	51 (18.6%)	51 (18.6%)	114 (41.6%)
Total	50	137	87	274

Serial monitoring results were also analyzed on a per-patient basis as shown below. Concordances and exact Binomial 95% CI were determined.

| Elecsys | Change in Disease State | | |
Changes in CA 19-9	Progression	No Progression	Total
Increase >15%	41	29	70
No Significant Increase	6	13	19
Total	47	42	89

Positive concordance = 0.872 (41/47) (95% CI: 0.768, 0.938)
Negative concordance = 0.309 (13/42) (95% CI: 0.195, 0.445)
Total concordance = 0.607 (54/89) (95% CI: 0.498, 0.709)

| Predicate | Change in Disease State | | |
Changes in CA 19-9	Progression	No Progression	Total
Increase >15%	41	29	70
No Significant Increase	6	13	19
Total	47	42	89

Positive concordance = 0.872 (41/47) (95% CI: 0.768, 0.938)
Negative concordance = 0.309 (13/42) (95% CI: 0.195, 0.445)
Total concordance = 0.607 (54/89) (95% CI: 0.498, 0.709)
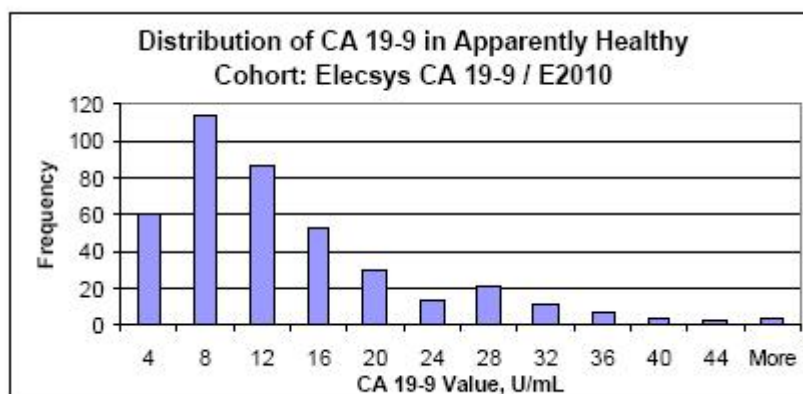
4. Clinical cut-off:
   Not applicable.
5. Expected values/Reference range:
   The normal reference range was established by testing serum samples from 403 apparently healthy subjects (200 females and 203 males) collected during routine physician visits from 11 centers. The cohort consisted of 366 Caucasians, 18 African Americans, 16 Hispanics, 2 Asians and 1 Native American. The mean and median age of the cohort was 56.2y (ranged from 40y to 88y) and 54.7y respectively. The female subjects had a mean age of 56y (40y to 88y) and median age of 54.3y whereas the mean age of the male subjects was 56.5y (40y to 88y) and median age 55y. The mean ages between the genders were not statistically different. Overall mean specimen age was 2.23y (ranged from 1.5 to 3.58y) with a median value of 1.91y. Of the 403 specimens, 96 were 3 to 3.58y old. The table below shows the CA 19-9 results analyzed by gender.

Subject	#Subjects	CA 19-9 Concentration (U/mL)		
		Mean ± SD	Median	Range
Males	203	10.65 ± 10.02	7.72	0.0-50.22
Female	200	11.03 ± 9.80	8.57	0.0-64.49
Combined	403	10.84 ± 9.9	8.23	0.0-64.49

Confidence intervals for the 5th, 90th and 95th order statistics were constructed using a resampling technique in validated SAS-Macros (Version 8.2). Approximate 95% confidence intervals (CI) were developed by identification of the value of CA 19-9 at the 2.5th and 97.5th percentiles of the sampling distribution. An estimate for the upper limit of normal (ULN) based on the 97.5% quantile is 35.07 U/mL with a 95% CI of 30.56-42.05 U/mL. Results were comparable to that of the predicate device (36.18 U/mL, 95%CI 34.11-41.17 U/mL). The following histogram shows the distribution of CA 19-9 in the normal cohort.

Distribution of CA 19-9 in Apparently Healthy Cohort: Elecsys CA 19-9 / E2010

In addition to the normal cohort, 456 serum samples from patients with benign conditions (192 females and 264 males) and 456 from patients (232 females and 262 males) with malignant diseases were tested. The benign disease samples were collected from 22 centers and selection was based on presenting symptoms, previous test results or diagnosis. The benign cohort consisted of 399 Caucasians, 48 African Americans, 8 Hispanics and 1 Asians. The overall mean age and median age were 62y (ranged from 40y to 92y) and 63y respectively. The female subjects had a mean age of 61.4y (40y to 88y) and median age of 62y and the mean age of the male subjects was 62.4y (40y to 92y) and median age 63y. Overall mean specimen age was 3.09y (ranged from 1.58 to 5.75y) with a median value of 3.17y. Of the 456 specimens, 383 were older than 3y

The specimens from malignant subjects were from 3 collection sites. The malignant cohort consisted of 383 Caucasians, 33 African Americans, 54 Hispanics, 23 Asians and 1 other. The overall mean age and median age were 60y (ranged from 24y to 86y) and 61y respectively. The female subjects had a mean age of 60 y (24y to 86y) and median age of 61y and the mean age of the male subjects was 61y (25y to 86y) and median age 60y. Overall mean

specimen age for the malignant group was 5.81y (ranged from 0.08 to 9.58y) with a median value of 6.5y. The Elecsys CA 19-9 results concentrations for the cohorts are summarized below.

Cohorts	# Subjects	Elecsys CA 19-9 concentration U/mL			
		Mean ± SD	Median	Range	% > 35
Benign Disease					
Heart Disease	98	11.6 ± 9.22	8.7	0.0-41.1	4.1
Pancreatic	100	18.8 ± 12.7	16.0	0.0-57.5	15.0
Gastrointestinal	145	15.4 ± 16.3	9.6	0.0-125.8	9.0
Genitourinary	113	17.1 ± 13.56	13.8	0.0-81.6	8.9
Total	456	15.7 ± 13.74	11.8	0.0-125.8	9.2
Malignant Disease					
Breast/Ovarian/Cervical	70	30.3 ± 69.28	14.2	1.92-569.2	15.71
Colorectal	228	370.2 ± 1,897.77	23.6	0.0-23,790	40.35
Esophageal/Gastric	29	19.9 ± 45.12	9.0	1.8-248.0	6.89
Gall bladder/Biliary	30	1,441 ±	210.9	0.75-13,830	63.33
Liver	54	96.5 ± 260.91	33.6	0.0-1,853	46.29
Lung	46	34.9 ± 55.17	16.3	1.26-335.4	26.09
Pancreatic	37	5,611 ± 16,584	196.2	1.17-80,780	75.67

The table below shows the bootstrapped 95% CI for the 95th order statistics for the benign and malignant disease groups of the predicate and test device. Bootstrap samples were obtained by resampling (with replacement) values of the devices by subject. Results indicate that at the 95th order statistics, there is no difference between the predicate and test device.

Cohorts	Predicate		Elecsys	
	CA 19-9	95% CI (U/mL)	CA 19-9 (U/mL)	95% CI (U/mL)
Benign Disease				
Heart Disease	34.17	22.69-38.37	32.76	24.58-55.82
Pancreatic	64.48	43.96-74.69	41.65	36.17-52.08
Gastrointestinal	47.82	31.83-61.91	46.65	31.81-59.79
Genitourinary	43.20	34.47-55.78	41.84	33.00-59.91
Total	50.82	41.17-59.66	40.15	36.23-48.28
Malignant Disease				
Breast/Ovarian/Cervical	99.6	61.0-302.8	81.9	42.3-107.1
Colorectal	1,972	1,006-10,757	1,185	480-2,820
Esophageal/Gastric	26.6	17.2-786.6	38.6	20.7-248.5
Gall bladder/Biliary	23,242	4,817-43,795	8,716	1,753-13,830
Liver	151.6	68.5-674.1	297.9	117.4-978.1
Lung	152.1	66.4-524.3	11.7	55.0-291.0
Pancreatic	56,604	18,989-174,340	28,132	7,146-80,780

The following table summarizes the distribution of subjects according to Elecsys CA 19-9 concentrations. Results showed all cancer groups had higher mean CA 19-9 values than the benign disease cohorts. The pancreatic cancer and the gall bladder/biliary cancer groups had the highest mean values.

Cohorts	# Subjects	Elecsys CA 19-9 Concentrations (U/mL)					
		0-35	35.1-70	70.1-200	201-2000	2001-20000	>20000
Apparently Healthy	403	392 (97.3%)*	10 (2.5%)	1 (0.2%)			
Benign Conditions							
Genitourinary	113	103 (91.2%)	9 (8%)	1 (0.9%)			
Gastrointestinal	145	132 (91.0%)	12 (8.3%)	1 (0.7%)			
Cardiac	98	94 (95.9%)	4 (4.1%)				
Pancreatic	100	85 (85%)	15 (15%)				
Malignant Conditions							
Breast/Ovarian/Cervical	70	58 (82.9%)	7 (10%)	4 (5.7%)	1 (1.4%)		
Colorectal	228	133 (58.3%)	27 (11.8%)	27 (11.8%)	34 (14.9%)	6 (2.6%)	1 (0.4%)
Esophageal/Gastric	29	26 (89.7%)	2 (6.9%)		1 (3.4%)		
Gall bladder/Biliary	30	11 (36.7%)		1 (3.3%)	14 (46.7%)	4 (13.3%)	
Liver	54	28 (51.9%)	12 (22.2%)	10 (18.5%)	4 (7.4%)		
Lung	46	34 (73.9%)	7 (15.2%)	4 (8.7%)	1 (2.2%)		
Pancreatic	37	9 (24.3%)	4 (10.8%)	6 (16.2%)	10 (27%)	6 (16.2%)	2 (5.4%)

*Percentage of population

Distribution of subjects according to the predicate CA 19-9 results is shown below.

Cohorts	# Subjects	Predicate CA 19-9 Concentrations (U/mL)					
		0-37	37.1-70	70.1-200	201-2000	2001-20000	>20000
Apparently Healthy	403	387 (96%)*	16 (4%)				
Benign Conditions							
Genitourinary	113	103 (91.2%)	9 (8%)	1 (0.9%)			
Gastrointestinal	145	132 (91.0%)	10 (6.9%)	3 (2.1%)			
Cardiac	98	93 (94.9%)	4 (4.1%)	1 (1%)			
Pancreatic	100	81 (81%)	14 (14%)	5 (5%)			
Malignant Conditions							
Breast/Ovarian/Cervical	70	48 (68.6%)	14 (20%)	6 (8.6%)	2 (2.9%)		
Colorectal	228	129 (56.6%)	20 (8.8%)	35 (15.4%)	33 (14.5%)	9 (3.9%)	2 (0.9%)
Esophageal/Gastric	29	28 (96.6%)			1 (3.4%)		
Gall bladder/Biliary	30	8 (26.7%)	2 (6.7%)	2 (6.7%)	9 (30%)	9 (23.3%)	2 (6.7%)
Liver	54	39 (72.2%)	8 (14.8%)	5 (9.3%)	2 (3.7%)		
Lung	46	32 (69.6%)	8 (17.4%)	4 (8.7%)	2 (4.3%)		

Cohorts	#	Predicate CA 19-9 Concentrations (U/mL)					
	Subjects	0-37	37.1-70	70.1-200	201-2000	2001-20000	>20000
Pancreatic	37	11 (29.7%)	2 (5.4%)	5 (13.5%)	8 (21.6%)	5 (13.5%)	6 (16.2%)

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.