510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K213510

B Applicant

Siemens Healthcare Diagnostics Products Ltd

C Proprietary and Established Names

IMMULITE/IMMULITE 1000 OM-MA
IMMULITE 2000 OM-MA

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LTK	Class II	21 CFR 866.6010 - Tumor-Associated Antigen Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

Modification of the previously cleared device to reduce biotin interference

B Measurand:

Cancer Antigen 125 (CA 125)

C Type of Test:

Quantitative, chemiluminescent immunometric assay

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

III Intended Use/Indications for Use:

A Intended Use(s):

IMMULITE/IMMULITE 1000 OM-MA
For in vitro diagnostic use with the IMMULITE and IMMULITE 1000 Analyzers — for the quantitative measurement of CA125 antigen in serum, as an aid in monitoring the response to therapy for patients with epithelian ovarian cancer, and in detecting residual ovarian cancer in patients who have undergone first-line therapy and would be considered for diagnostic second look procedures.

IMMULITE 2000 OM-MA
For in vitro diagnostic use with the IMMULITE 2000 Systems Analyzers — for the quantitative measurement of CA125 antigen in serum, as an aid in monitoring the response to therapy for patients with epithelian ovarian cancer, and in detecting residual ovarian cancer in patients who have undergone first-line therapy and would be considered for diagnostic second-look procedures.

B Indication(s) for Use:

Same as Intended Use

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The package insert of the devices contains the warning: "CA125 antigen levels in a given specimen determined with assays from different manufacturers can vary due to differences in assay methods and reagent specificity. Results reported by the laboratory to the physician must include the identity of the assay used to measure CA125 antigen levels. Values obtained with different assays cannot be used interchangeably. Before changing assays, the laboratory must confirm baseline values for patients being serially monitored."

D Special Instrument Requirements:

For use with the IMMULITE/IMMULITE 1000 (K022603) and IMMULITE 2000 Systems Analyzers (K970227)

IV Device/System Characteristics:

A Device Description:

IMMULITE/IMMULITE 1000 OM-MA kit contains the following:

- OM-MA Test Units (100 units): each unit contains one bead coated with murine monoclonal anti-CA125 antibody
- OM-MA Reagent Wedge
    - Cycle 1 Reagent Wedge (7.5 mL): alkaline phosphatase (bovine calf intestine) conjugated to rabbit polyclonal anti-CA125 antibody in buffer, with preservative

    - Cycle 2 Reagent Wedge (5 mL): buffer, with preservative
- OM-MA Adjustors (Low and High; 2 vials, 3 mL/vial): CA125 in a nonhuman protein/buffer matrix, with preservative, each.

IMMULITE 2000 OM-MA kit contains the following:

- OM-MA Bead Pack (1 pack, 200 beads/pack): coated with murine monoclonal anti-CA125 antibody
- OM-MA Reagent Wedge (1 wedge):
    - Well 1 (11.5 mL): alkaline phosphatase (bovine calf intestine conjugated to rabbit polyclonal anti-CA125 antibody in buffer, with preservative
    - Well 2 (6.5 mL): buffer, with preservative
- OM-MA Adjustors (Low and High; 2 vials, 3 mL/vial): CA125 in a nonhuman protein/buffer matrix, with preservative

Materials Required but not provided:

- Chemiluminescent Substrate
- OM-MA Sample Diluent
- Probe Wash
- Probe Cleaning Kit

The manufacturer recommends the use of commercially available quality control materials or sample pools with at least two levels (low and high) of CA125.

IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA has been modified from the previously cleared assay which is susceptible to interference from biotin. The modification was made to add additional biotin to blocking buffer during solid phase manufacturing, which eliminates the risk of biotin interference.

B Principle of Operation:

The IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA are solid-phase chemiluminescent immunometric assays. The solid phase consists of polystyrene latex beads coated with anti-CA 125 antibody (Ab). The patient sample incubated with beads and alkaline phosphatase antibody conjugate which results in a bead pair immunocomplex sandwich consisting of capture Ab-antigen-detection Ab (30-minute incubation cycle). Next, a wash buffer is added to remove unbound conjugate (30-minute cycle). Unbound conjugate is removed by centrifugal wash, following by addition of chemiluminescent substrate to the beads and incubated for 10 minutes. The chemiluminescent substrate undergoes hydrolysis in the presence of the alkaline phosphatase to yield an unstable intermediate, which then emits photons. The sustained emissions are measured by the luminometer. The resulting relative light units (RLU) are proportional to the concentration of CA 125 in the sample, which is expressed as U/mL.

V Substantial Equivalence Information:

A Predicate Device Name(s):

IMMULITE OM-MA, MODELS LKOPZ, LKOP1, LKOP5;
IMMULITE 2000 OM-MA MODEL L2KOP2

B Predicate 510(k) Number(s):

K981297
K983391

C Comparison with Predicate(s):

Device & Predicate Device(s):	K213510 New Device	K981297 Predicate	K983391 Predicate
Device Trade Name	IMMULITE/IMMULITE 1000 OM-MA IMMULITE 2000 OM-MA	IMMULITE OM-MA	IMMULITE 2000 OM-MA
General Device Characteristic Similarities			
Intended Use / Indications for Use	For in vitro diagnostic use with the IMMULITE and IMMULITE 1000 Analyzers — for the quantitative measurement of CA125 antigen in serum, as an aid in monitoring the response to therapy for patients with epithelian ovarian cancer, and in detecting residual ovarian cancer in patients who have undergone first-line therapy and would be considered for diagnostic second look procedures. For in vitro diagnostic use with the IMMULITE 2000 Systems Analyzers — for the quantitative measurement of CA125 antigen in serum, as an aid in monitoring the response to therapy for patients with epithelian ovarian cancer, and in detecting residual ovarian cancer in patients who have undergone first-line therapy and would be considered for diagnostic second-look procedures.	Same	Same
Analyte	Cancer Antigen 125	Same	Same
Automated	Automated assay	Same	Same
Type of test	Quantitative	Same	Same
Assay technology	Chemiluminescent	Same	Same
Sample matrix	Serum	Same	Same
Sample volume	50 µL	Same	Same
Capture antibody	Murine monoclonal Anti-CA 125 antibody	Same	Same
Detection antibody	Bovine alkaline phosphatase conjugated to rabbit polyclonal antibody	Same	Same
Calibration	Two-point, up to 500 U/mL (Adjusters)	Same	Same

Controls	Commercially available, minimum of two levels	Same	Same
Instrument	IMMULITE/ IMMULITE 1000 and IMMULITE 2000 Systems Analyzers	Same	Same
Shelf life	12 months	Same	Same
Cut-off	Normal: < 21 U/mL Elevated: > 21 U/mL	Same	Same
General Device Characteristic Differences			
Assay Modification	Modified solid phase	Unmodified solid phase	
Analytical sensitivity	IMMULITE/IMMULITE 1000 OM-MA: LoB: 0.14 U/mL LoD: 0.38 U/mL LoQ: 2.00 U/mL IMMULITE 2000 OM-MA: LoB: 0.18 U/mL LoD: 0.43 U/mL LoQ: 3.00 U/mL	LoD: 1 U/mL	
Measuring range	IMMULITE/IMMULITE 1000 OM-MA: 2 – 500 U/mL IMMULITE 2000 OM-MA: 3 – 500 U/mL	1 – 500 U/mL	

VI Standards/Guidance Documents Referenced:

The following Clinical and Laboratory Standards Institute (CLSI) guidelines were used:

- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures, Approved Guideline – Third Edition
- CLSI EP06-Ed2, Evaluation of the Linearity of Quantitative Measurement Procedures
- CLSI EP07, Interference Testing in Clinical Chemistry – Third Edition
- CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline
- CLSI EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, Approved Guideline – Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility: The studies were performed following CLSI EP05-A3.

Within-laboratory precision

Five serum samples were assayed in two replicates per sample per run, two runs per day for 20 days using one lot of reagents on one instrument (N=80 per sample). Sample 1 was native serum sample, and Samples 2–5 were pooled samples prepared by pooling high CA 125 serum samples with low CA 125 serum samples. The data was analyzed using ANOVA for standard deviation (SD), % coefficient of variation (%CV) to evaluate within-run, between-run, between-day, and within-laboratory. The results are summarized below:

IMMULITE/IMMULITE 1000 OM-MA

Sample	Mean (U/mL)	Within-Run		Between-Run		Between-Day		Within-Lab	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	9.17	0.41	4.5	0.26	2.8	0.00	0.0	0.49	5.3
2	19.21	0.86	4.5	0.31	1.6	0.28	1.5	0.95	5.0
3	41.36	1.38	3.3	0.98	2.4	0.54	1.3	1.77	4.3
4	225.95	8.87	3.9	2.88	1.3	1.28	0.6	9.41	4.2
5	427.48	12.40	2.9	2.99	0.7	1.61	0.4	12.86	3.0

IMMULITE 2000 OM-MA

Sample	Mean (U/mL)	Within-Run		Between-Run		Between-Day		Within-Lab	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	11.23	0.59	5.2	0.33	3.0	0.07	0.6	0.68	6.0
2	23.69	1.45	6.1	1.09	4.6	0.00	0.0	1.82	7.7
3	42.59	1.86	4.4	1.14	2.7	0.20	0.5	2.19	5.1
4	226.17	10.57	4.7	3.36	1.5	3.59	1.6	11.66	5.2
5	451.54	22.58	5.0	14.47	3.2	0.00	0.0	26.82	5.9

Lot-to-lot imprecision

Five serum samples were used for the study, Sample 1 was native serum sample, and Samples 2–5 were pooled samples prepared by pooling high CA 125 serum samples with low CA 125 serum samples. Three lots of IMMULITE/IMMULITE 1000 OM-MA and three lots of IMMULITE 2000 OM-MA were assayed on one instrument (per platform), on each of five days, with five replicates per sample per run per day. The data was analyzed using ANOVA for SD, %CV to evaluate within-run (repeatability), between-day, between-lot, reproducibility (total precision). The results are summarized in the tables below:

IMMULITE/IMMULITE 1000 OM-MA

Sample	Mean (U/mL)	Within-Run		Between-Run		Between-Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	9.41	0.45	4.80	0.17	1.77	0.54	5.73	0.78	8.33
2	18.72	1.25	6.66	0.25	1.35	1.21	6.45	1.75	9.37
3	39.68	2.35	5.91	1.07	2.70	2.53	6.38	3.64	9.18
4	215.20	10.87	5.05	0.00	0.00	11.30	5.25	16.24	7.55
5	420.97	24.65	5.86	7.95	1.89	25.32	6.02	37.57	8.93

IMMULITE 2000 OM-MA

Sample	Mean (U/mL)	Within-Run		Between-Run		Between-Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	11.26	0.50	4.45	0.27	2.40	0.53	4.66	0.81	7.15
2	22.94	1.23	5.36	0.54	2.37	1.13	4.94	1.76	7.66
3	40.49	2.18	5.37	0.00	0.00	1.34	3.30	2.64	6.52
4	213.03	11.79	5.53	4.23	1.99	4.02	1.89	13.18	6.19
5	425.82	27.13	6.37	9.80	2.30	18.49	4.34	33.43	7.85

2. Linearity:

The linearity study was conducted following CLSI EP06-Ed2. A panel of nine samples was prepared by mixing high serum native sample with a low native serum sample to cover the claimed analytical measuring range of each of two assays, IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA. For each assay, the samples were tested on four replicates per sample using three reagent lots of each assay on one instrument. The data was analyzed using weighted least squares linear regression. Percent deviations from linearity were calculated as differences between the observed values (mean values) and the predicted values divided by the predicted values. Results are summarized below.

IMMULITE/IMMULITE 1000 OM-MA

Kit Lot	Dilution Range (U/mL)	Slope (95% CI)	Intercept (95% CI)	R^2	% Deviation from Linearity
1	2.07 – 423.08	1.06 (1.01 – 1.11)	-0.11 (-0.39 – 0.18)	1.00	0.8% – 6.4 %
2	2.32 – 424.77	1.09 (1.05 – 1.13)	-0.18 (-0.40 – 0.03)	1.00	0.1% – 8.0%
3	2.09 – 426.13	1.09 (1.05 – 1.12)	-0.15 (-0.49 – 0.18)	1.00	0.1% – 7.8%

IMMULITE 2000 OM-MA

Kit Lot	Dilution Range (U/mL)	Slope (95% CI)	Intercept (95% CI)	R^2	% Deviation from Linearity
1	2.51 – 665.80	1.02 (0.98 – 1.05)	-0.00 (-0.30 – 0.30)	1.00	0.4% – 11.4%
2	2.28 – 613.91	1.13 (1.08 – 1.18)	-0.26 (-0.65 – 0.13)	1.00	0.1% – 11.7%
3	2.50 – 573.55	1.12 (1.07 – 1.17)	-0.22 (-0.65 – 0.20)	1.00	0.4% – 10.7%

The study results support the linearity of the claimed measuring interval 2 – 500 U/mL for IMMULITE/IMMULITE 1000 OM-MA and 3 – 500 U/mL for IMMULITE 2000 OM-MA.

Automatic dilution versus manual dilution (IMMULITE 2000)

To verify the auto-dilution function on IMMULITE 2000 instrument platform, one high sample (> 500U/mL) was diluted using the onboard dilution function and compared with dilution of the same sample that was manually diluted by the same dilution factor. The high native serum pool was diluted using assay diluent 10x, 20x and 40x. The study was conducted on three kit lots of the modified IMMULITE 2000 OM-MA kits on one IMMULITE 2000 platform. The dose by onboard dilution was compared to the dose obtained by manual dilution and % bias calculated and compared to the acceptance criteria. The study results demonstrated % bias within 10%.

Hook Effect

Hook effect was evaluated by testing samples above the analytical measuring interval: from 500 to 146,000 U/mL. Three lot of reagents of each IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA were used. The results showed no hook effect up to 84,500 U/mL for IMMULITE/IMMULITE 1000 OM-MA and up to 80,000 U/mL for IMMULITE 2000 OM-MA.

3. Analytical Specificity/Interference:

Cross-reactivity

The cross-reactivity of the modified IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA assays with AFP, CA15-3, CA19-9, and CEA was evaluated by testing two patient sample pools at low level (between 8–12 U/mL) and one at a mid-level close to the cut-off (between 17–25 U/mL). Each substance was spiked into test samples, and control samples were prepared by spiking solvent into the samples. Samples were run in replicates of five using three lots of the modified IMMULITE/IMMULITE 1000 OM-MA, and three lots of the modified IMMULITE 2000 OM-MA. The results confirmed that the modified devices have the same cross reactivity information for AFP, CA15-3, CA19-9 and CEA as presented in K981297 and K983391, respectively. The package insert has the following table for the cross reactivity:

Compound	Concentration
AFP	10,000 IU/mL
CA15-3*	1753 U/mL
CA19-9	4000 U/mL
CEA**	10,000 ng/mL

*Cross-reactivity at 0.41% at analyte concentration of 7.1 U/mL
**Cross-reactivity at 0.05% at analyte concentration of 4.8 U/mL

Interference

The interference of the modified IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA assays was performed following recommendations of CLSI EP07, 3rd ed.

Human Anti-Mouse Antibodies (HAMA) interference was evaluated by testing two patient sample pools at ~35 U/mL and ~175 U/mL. The samples were spiked with the commercially available HAMA Serum Type I (2680 µg/L) and HAMA Serum Type II (3960 µg/L). The samples were assayed in duplicate on one lot of modified IMMULITE/IMMULITE 1000 OM-MA and two lots of modified IMMULITE 2000 OM-MA.

Alkaline phosphatase interference was evaluated by testing three patient sample pools with CA 125 level at ~10 U/mL, ~21 U/mL, and ~100 U/mL. Alkaline phosphatase was spiked into test samples to attain a concentration of 700 U/L, control samples were spiked with solvent used for preparation of test samples. Samples were run in replicates of five on three lots of modified IMMULITE/IMMULITE 1000 OM-MA, and three lots of modified IMMULITE 2000 OM-MA.

Bilirubin (conjugated and unconjugated), hemoglobin, intralipid (triglycerides), and biotin interference was evaluated by testing two patient sample pools at low level (~17 U/mL) and high level (~185 U/mL). Control samples were prepared by spiking of the solvent used to prepare the test substance into patient sample pools. Test samples were prepared by spiking working stocks containing the different interferent materials. Samples were run on one lot of modified IMMULITE/IMMULITE 1000 OM-MA, and two lots of modified IMMULITE 2000 OM-MA.

The results for all interference studies were evaluated by calculation % bias between control and test samples. No significant interferences were observed up to the concentrations listed in the table below:

Compound	Concentration
HAMA	792 µg/L
Alkaline phosphatase	700 U/L
Conjugated Bilirubin	200 mg/L
Unconjugated Bilirubin	200 mg/L
Hemoglobin	381 mg/dL for IMMULITE/IMMULITE 1000 OM-MA 192 mg/dL for IMMULITE 2000 OM-MA
Intralipid (Triglycerides)	3000 mg/dL
Biotin	3500 ng/mL

4. Assay Reportable Range:

IMMULITE/IMMULITE 1000 OM-MA: 2 – 500 U/mL
IMMULITE 2000 OM-MA: 3 – 500 U/mL

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Traceability

The assay is traceable to an internal standard, no international reference standard is available for CA 125 at this time.

Stability

The shelf-life of the modified reagents were tested using the representative assay, IMMULITE 2000 OM-MA assay. The study was performed following CLSI EP25-A. Three native serum sample pools at ~10 U/mL, ~21 U/mL, and ~100 U/mL were prepared and conditioned by stressing the kits over a period of 30 days at the following temperatures: 15, 25 and 37 °C. Three lots of each of the modified reagent kits were stored over a period of 30 days at the following temperatures: 15, 25 and 37 °C, and assayed at the following timepoints: 0, 6, 12, 18, 24 and 30 days, using one IMMULITE 2000 instrument. The results were analyzed by calculation first-order degradation kinetics using the Arrhenius equation approach. The study results supported kit stability for 365 days at 2–8 °C.

6. Detection Limit:

Limit of blank (LoB), limit of detection (LoD) and limit of quantitation (LoQ) was established for IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA following recommendations of CLSI EP17-A2.

The LoB was determined from the measurement of four analyte-free serum samples tested in six replicates per sample over three days using two reagent lots. LoB was calculated using the classical non-parametric approach by establishing the 95% rank.

The LoD was determined from the measurement of five native low-level samples in five replicates, two runs per day over five days using two lots of reagents on two instruments. LoD was calculated as the LoB + 1.645 x SD of the replicates for the low level samples.

The LoQ was determined based on the LoD study described above using the precision profile. LoQ was defined as the level meet the %CV of the within-lab imprecision of 20%.

The results are summarized in table below:

	IMMULITE/IMMULITE 1000 OM-MA	**IMMULITE 2000 OM-MA**
LoB	0.14 U/mL	0.18 U/mL
LoD	0.38 U/mL	0.43 U/mL
LoQ	2.00 U/mL	3.00 U/mL

7. Assay Cut-Off:

Assay cut-off was established in K981297and K983391.

Decision Point	**Interpretation**
< 21 U/mL	Normal
> 21 U/mL	Elevated

B Comparison Studies:

1. Method Comparison with Predicate Device:

IMMULITE/IMMULITE 1000 OM-MA

A total of 253 native serum samples were tested one run per sample over eight days using three lots of the modified IMMULITE/IMMULITE 1000 OM-MA and one lot of the predicate device (K981297) on one IMMULITE platform. The samples included 103 samples from patients with ovarian cancer, 35 samples from patients with non-ovarian cancer (20 prostate cancer, 15 breast cancer), 40 samples from patients with nonmalignant diseases (12 gastrointestinal disease, 4 fibroma, 3 adenoma, 21 genitourinary), 50 samples from healthy females (25 pre-menopausal, 25 post-menopausal), and additional 25 contrived samples to cover the upper end of the measuring range. The contrived samples were prepared by mixing high CA 125 native samples (5% by volume) into low CA 125 native samples. Only the samples within the measuring ranges of both the modified device and the predicate were analyzed by Passing-Bablok regression, and the results are summarized below:

Lot #	N	Range (U/mL)	Slope (95% CI)	Intercept (95% CI)	R
1	246	1.03 – 466	0.995 (0.984 – 1.012)	-0.199 (-0.339 – 0.039)	0.994
2	246	1.68 – 455	0.999 (0.988 – 1.013)	-0.047 (-0.211 – 0.175)	0.995
3	247	1.27 – 471	1.022 (1.011 – 1.035)	-0.821 (-0.962 – -0.574)	0.994

IMMULITE 2000 OM-MA

The same samples described above were tested one run per sample on one day using three lots of the modified IMMULITE 2000 OM-MA and one lot of the predicate device (K983391) on one IMMULITE 2000 platform. Only the samples within the measuring ranges of both the modified device and the predicate were analyzed by Passing-Bablok regression, and the results are summarized below:

Lot #	N	Range (U/mL)	Slope (95% CI)	Intercept (95% CI)	R
1	246	2.47 – 511	1.032 (1.021 – 1.045)	0.086 (-0.163 – 0.241)	0.995
2	246	2.11 – 525	0.955 (0.941 – 0.963)	-0.256 (-0.445 – -0.038)	0.994
3	246	2.29 – 489	0.976 (0.963 – 0.992)	-0.142 (-0.340 – 0.097)	0.995

2. Matrix Comparison:

Not applicable

C Clinical Studies:

Clinical studies were conducted in K981297 and K983391.

D Clinical Cut-Off:

Clinical cut-offs were established in K981297 and K983391.

E Expected Values/Reference Range:

To verify the reference range of the modified IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA remaining the same as that established in K981297 and K983391, a total of 50 samples (21 pre-menopausal and 29 post-menopausal female) from apparently healthy female individuals were tested by following recommendations of CLSI EP28-A3c. Samples were from subjects representing three major ethnic groups (16 Caucasian, 16 African-American, and 34 Asian). The samples were run in duplicate, three lots of each of the modified reagent kits on each platform (six lots total). Five samples were excluded due to insufficient volume, three samples were found elevated (greater than 21 U/mL). The results are summarized in the Table below.

IMMULITE/IMMULITE 1000 OM-MA

	Lot 1	Lot 2	Lot 3*
n	50	50	45
n < 21 U/mL	47	47	42
% < 21 U/mL	94%	94%	93%

* five samples were not tested due to insufficient sample volume

IMMULITE 2000 OM-MA

	Lot 1	Lot 2	Lot 3
n	50	50	50
n < 21 U/mL	47	47	47
% < 21 U/mL	94%	94%	94%

The result supports that there is no change of reference range established previously in K981297 and K983391 for the modified IMMULITE/IMMULITE 1000 OM-MA and IMMULITE 2000 OM-MA.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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