U.S. FOOD & DRUG ADMINISTRATION

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K231601

B Applicant

Sebia

C Proprietary and Established Names

FLC Kappa
FLC Lambda

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DFH DEH	Class II	21 CFR 866.5550 - Immunoglobulin (Light Chain Specific) Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

Modification of previously cleared devices – addition of intended use as aid in monitoring of multiple myeloma and AL amyloidosis and extension of shelf-life of kit and controls

B Measurand:

Kappa (κ) Free Light Chain (FLC)
Lambda (λ) Free Light Chain (FLC)

C Type of Test:

Manual enzyme-linked immunosorbent assay (ELISA), Quantitative

III Intended Use/Indications for Use:

A Intended Use(s):

The FLC Kappa kit is intended for the quantification of Kappa free light chains in human serum from adults with an Enzyme-Linked Immunosorbent Assay (ELISA) procedure. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma and AL amyloidosis. It must be used in conjunction with other laboratory and clinical findings.
For In Vitro Diagnostic Use only.

The FLC Lambda kit is intended for the quantification of Lambda free light chains in human serum from adults with an Enzyme-Linked Immunosorbent Assay (ELISA) procedure. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma and AL amyloidosis. It must be used in conjunction with other laboratory and clinical findings.
For In Vitro Diagnostic Use only.

B Indication(s) for Use:

Same as intended use

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Warning: The result of the FLC Kappa in a given specimen determined with assays and/or instrument platforms from different manufacturers can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of serially monitoring a patient, the assay method used for determining the FLC Kappa level is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

D Special Instrument Requirements:

This is a manual ELISA and there are no special instrument requirements.

IV Device/System Characteristics:

A Device Description:

The FLC Kappa is comprised of the following reagents:

- Kappa microplate: coated with polyclonal rabbit anti-human kappa FLC antibody
- Dilution Buffer
- Wash Solution
- Anti-Kappa Antiserum
- Stop Solution

- Calibrators: A five level set in liquid form with target concentrations: 2.7 mg/L, 5.3 mg/L 16 mg/L, 48 mg/L and 96 mg/L, ready to use.

The FLC Lambda is comprised of the following reagents:

- Lambda Microplate: coated with polyclonal rabbit anti-human lambda FLC antibody
- Dilution Buffer
- Wash Solution
- Anti-Lambda Antiserum
- Stop Solution
- Calibrators: A five level set in liquid form with target concentrations: 2.9 mg/L, 5.9 mg/L, 17.7 mg/L, 53.0 mg/L and 106.0 mg/L, ready to use.

The following materials are required but not provided in the kits:

- Densitometer for microplate reading by absorbance spectrophotometry at 450 nm.
- FLC Control Level 1 with target concentrations for Kappa: 9–25 mg/L and Lambda: 15–30 mg/L
- FLC Control Level 2 with target concentrations for Kappa and Lambda > 35 mg/L

FLC Control Level 1 and FLC Control Level 2 are intended for the quality control of SEBIA immunoenzymatic procedures and are obtained from a pool of human sera. The controls are packaged in a stabilized lyophilized form. It must be noted that the high limit of the FLC Control Level 2 must not exceed the values of the Calibrator 5. Additionally, the exact concentrations for FLC Control Level 1 and FLC control Level 2 are lot dependent.

B Principle of Operation:

The FLC Kappa and FLC Lambda assays are intended for the quantification of FLCs in human serum from adults with an Enzyme-Linked Immunosorbent Assay (ELISA) procedure utilizing specific anti-Kappa and anti-Lambda FLC antibodies. Kappa FLC or Lambda FLC in the sample binds to specific anti-Kappa FLC antibody or anti-Lambda FLC antibody coated on the wells of microplates. Following the washing step, the samples in wells are incubated with an anti-FLC antiserum (Kit specific) conjugated to horseradish peroxidase followed by another washing of wells to remove the excess of the conjugated antiserum. Reading of the optical density is performed by absorbance spectrophotometry at 450 nm of the colored product. Finally, the calculation of the FLC concentration of the sample is performed using a calibration curve obtained with calibrators that have been analyzed on the same microplate.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Freelite Human Kappa Free Kit and Freelite Human Lambda Free Kit for use on the Dade Behring Nephelometer II

B Predicate 510(k) Number(s):

K031016

C Comparison with Predicate(s):

Device & Predicate Device(s):	**K231601**	**K031016**
Device Trade Name	FLC Kappa FLC Lambda	Freelite Human Kappa Free and Freelite Human Lambda Free kits for use on the Siemens BN II
General Device Characteristic Similarities		
Analyte	Kappa FLC and Lambda FLC	Same
Measurement	Quantitative	Same
Intended Use/ Indications for Use	The FLC Kappa kit is intended for the quantification of Kappa free light chains in human serum from adults with an Enzyme-Linked Immunosorbent Assay (ELISA) procedure. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma and AL amyloidosis. It must be used in conjunction with other laboratory and clinical findings. For *In Vitro* Diagnostic Use only. The FLC Lambda kit is intended for the quantification of Lambda free light chains in human serum from adults with an Enzyme-Linked Immunosorbent Assay (ELISA) procedure. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma and AL amyloidosis. It must be used in conjunction with other laboratory and clinical findings. For *In Vitro* Diagnostic Use only.	Kappa: This kit is intended for the quantitation of kappa free light chains in serum and urine on the Siemens BN II. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings. Lambda: This kit is intended for the quantitation of lambda free light chains in serum and urine on the Siemens BN™ II. Measurement of free light chains aids in the diagnosis and monitoring of multiple myeloma, lymphocytic neoplasms, Waldenstrom's macroglobulinemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus in conjunction with other laboratory and clinical findings.
General Device Characteristic Differences		
Specimen Type	Human Serum	Human Serum, Human Urine
Detection Method	ELISA	Nephelometric

Capture Antibody	Polyclonal rabbit anti-human kappa/lambda FLC coated on the well of the microplate	Kappa: Polyclonal sheep anti-human kappa/lambda antibody coated with latex particles
Detection Antibody	Horseradish peroxidase (HRP) conjugated polyclonal rabbit anti-human kappa/lambda free light chain	Not appliable
Analytical Measuring Interval	Standard dilution (1/1000) Kappa: 4.5– 76.2 mg/L Lambda: 3.8 –66.8 mg/L	Standard dilution (1:100) Kappa: 0.3 –190 mg/L Lambda: 0.25–160 mg/L
Reference Interval	Kappa: 6.4 –17.4 mg/L. Lambda: 8.4 –21.8 mg/L. Ratio: 0.46 –1.51	Kappa: 3.3–19.4 mg/L Lambda: 5.7 –26.3 mg/L Ratio: 0.26–1.65
Calibrators	5-level	1-level
Controls (assigned values are lot dependent)	FLC Control Level 1: Kappa: 13.3 ± 6.7 mg/L Lambda: 22.2 ± 11.1 mg/L FLC Control Level 2: Kappa: 45.8 ± 22.9 mg/L Lambda: 44.2 ± 22.1 mg/L	Free Control: Kappa: 14.5–21.7 mg/L Lambda: 23.47–35.21 mg/L Free Control High: Kappa: 28.3–42.5 mg/L Lambda: 41.96 –62.94 mg/L

VI Standards/Guidance Documents Referenced:

Not applicable

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Refer to K210623

2. Linearity:

   Refer to K210623

3. Analytical Specificity/Interference:

   Refer to K210623

4. Assay Reportable Range:

   Refer to K210623

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

Traceability:

Refer to K210623

Stability:

Reagent Kit

a. Shelf-life stability: The real-time shelf-life stability of the FLC Kappa and FLC Lambda reagent kits was determined over a 13-month period using three reagent lots of each assay. Each reagent lot stored at 2–8ºC was tested at 0 (T0), 1, 2, 3, 4, 6, 9,10, 12 and 13 months. At each testing point, three serum samples (low, medium, and high concentration) as well as two controls (FLC Control Level 1 and FLC Control Level 2) were tested in triplicates using all three reagent lots of FLC Kappa and FLC Lambda, respectively. At each time point, the mean concentrations for Kappa and Lambda were compared to the initial target range concentration obtained at T0. The results are acceptable at all tested time points and hence support the shelf-life of FLC Kappa and FLC Lambda for 12 months at 2–8ºC.

b. Open-vial stability: Refer to K210623

FLC Controls

a. Shelf-life stability: The real-time stability of the FLC Control Level 1 and FLC Control Level 2 was determined over a three-year period using three lots. Each freeze-dried control stored at 2–8ºC was tested at 0 (T0), 12, 24 and 36 months. At each testing point, FLC Control Level 1 and FLC Control Level 2 were tested in triplicates using FLC Kappa and FLC Lambda, respectively. At each time point, the mean concentrations for Kappa and Lambda were compared to the initial target range concentration obtained at the zero-month (T0) time point. The results were acceptable at all tested time points and hence support the claimed shelf-life stability of the FLC Control Level 1 and FLC Control Level 2 up to 24 months at 2-8ºC.

b. In-use (reconstituted) stability: Refer to K210623

6. Detection Limit:

Refer to K210623

7. Assay Cut-Off:

Refer to K210623

B Comparison Studies:

1. Method Comparison with Predicate Device:

Refer to K210623

2. Matrix Comparison:

   Refer to K210623

C Clinical Studies:

Clinical performance of the Sebia FLC Kappa and the FLC Lambda assays as an aid in the diagnosis of multiple myeloma (MM) and as an aid in the diagnosis of AL amyloidosis was previously demonstrated in K210623.

Monitoring of multiple myeloma

1. Clinical Sensitivity and Clinical Specificity:
   The clinical performance of the Sebia FLC Kappa and FLC Lambda assays as an aid in monitoring of multiple myeloma (MM) patients was evaluated in serum samples from subjects diagnosed with MM during treatment and were compared to clinical response categories based on criteria from the International Myeloma Working Group (IMWG) guidelines. The patient inclusion and exclusion criteria were as follows:

   Inclusion criteria:
   - ≥18 years of age,
   - Adequate sample volume for testing
   - Confirmed diagnosis of MM at diagnosis time point
   - Samples from patients with 1 baseline time point and at least 2 follow-up time points
   - At least 20 samples with a "progressive" response criterion, and a significative representation of all the other responses criteria
   - The following information are needed for each sample:
     Age, sex, race, ethnicity of patient
     Time interval between 2 time points
     Treatment start/change date(s), use of chemotherapy or radiation treatment or bone marrow transplant (when available)
     Serum Protein Electrophoresis (SPEP) (M-spike)
     Serum IFE
   - Frozen samples (storage at -18/-30°C or -70/-80°C),
   - Less than 5 freeze-thaw cycles
   - Signed informed consent

   Exclusion criteria:
   - Patients with less than 2 follow-up points
   - Not enough collected information available to define the clinical status of the patient, based on the selected guidance to perform the classification
   - Missing FLC values at collection or at retest with the predicate or the candidate

   Of the 235 MM subjects, 77 subjects were diagnosed with IgG Kappa, 43 IgG Lambda, 21 IgA Kappa, 21 IgA Lambda, 6 IgM Kappa, 27 Light Chain Kappa MM, and 16 Light Chain Lambda MM. Six of the 235 subjects had two subtypes (clones) as follows: one IgG Kappa and IgA Kappa; one IgG Kappa and indeterminate heavy and light chain; one IgG Kappa and

normal heavy chain and indeterminate light chain; one IgA Kappa and IgM Kappa, and two IgG Lambda and Free Lambda light chain. Of the 136 MM subjects, 48 subjects were diagnosed with IgG Kappa, 23 IgG Lambda, 14 IgA Kappa, 10 IgA Lambda, 15 Kappa, and 9 Lambda.

Among 234 MM subjects, 139 (59%) were male and 96 (41%) were female. The median age was 64 years old with the age ranging from 33 to 88 years old. Most of the subjects were Caucasians (n=158; 67.2%). The remaining subjects were: African American (n=48; 20.4%,), Asian (n=14; 6.0%); Hispanic (n=12; 5.1%); Other (n=8; 3.4%); and Unknown (n=7; 3.0%). A total of 551 follow-up samples were tested by the Sebia Kappa FLC and Lambda FLC Assays. The duration of the monitoring days ranged from 10 days to 2729 days (with a median of 402 days).

The clinical assessment for each monitoring observation was determined according to IMWG Version 3.2021/National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology on Multiple Myeloma (Kumar et al., 2021). Clinical status of each monitoring event was categorized into one of six response categories: Stringent Complete Response (sCR), Complete Response (CR), Very Good Partial Response (VGPR), Partial Response (PR), Stable Disease (SD), and Progressive Disease (PD). The evaluation of patient response was regrouped into four categories: Good response (sCR and CR), Moderate Response (VGPR and PR), Stable Disease and Progressive Disease. Analysis was performed using these four categories. For each of 551 monitoring observations, the results of the Sebia Kappa and Lambda FLC assay in combination with other laboratory results were used to assign a response category and compared to the clinical assessment according to the following table:

<table>
<tr><th colspan="2">Response Criteria based on Sebia FLC, SPEP and IFE</th><th>Clinical Assessment based on IMWG</th></tr>
<tr><td rowspan="2">Good Response</td><td rowspan="2">(Normal FLC ratio, AND M-protein not detectable AND negative IFE)
OR
(M-protein not detectable AND negative IFE)</td><td>sCR</td></tr>
<tr><td>CR</td></tr>
<tr><td rowspan="2">Moderate Response</td><td rowspan="2">reduction in serum M-protein ≥ 50% AND
rd_dFLC decrease ≥ 50%</td><td>VGPR</td></tr>
<tr><td>PR</td></tr>
<tr><td>Stable Disease</td><td>Not meeting criteria for Good Response, Moderate Response, or Progressive Disease</td><td>SD</td></tr>
<tr><td>Progressive Disease</td><td>(≥ 25% increase of M-protein AND increase of M-protein ≥ 0.5 g/L)
OR
(≥ 25% increase of rd_dFLC AND d_dFLC increase > 100 mg/L</td><td>PD</td></tr>
</table>

- dFLC = involved FLC (monoclonal chain) – not involved FLC (polyclonal chain)
- rd_dFLC = (dFLC t2 - dFLC t1)/dFLC t1 (rd= relative difference; t1= time point 1; t2= time point 2)
- d_dFLC = dFLC t2 - dFLC t1 (d= absolute difference; t1= time point 1; t2= time point 2).

The clinical response criteria based on the Sebia FLC Kappa and FLC Lambda values were compared to the clinical response criteria based on the clinical assessment.

Response based on Sebia FLC assay	Clinical Assessment				
	Good Response*	Moderate Response^	Stable Disease	Progressive Disease	Total
Good Response*	78	0	0	1	79
Moderate Response^	0	82	14	0	96
Stable Disease	0	20	310	12	342
Progressive Disease	0	1	5	28	34
Total	78	103	329	41	551
Concordance (n/N) (95% CI)	100.0% (78/78) (100.0%;100.0%)	79.6% (82/103) (71.8%; 87.4%)	94.2% (310/329) (91.7%; 96.7%)	68.3% (28/41) (54.0%; 82.5%)	90.4% (498/551) (87.9%; 92.8%)

* Including subjects with Stringent CR and CR.
^ Including subjects with VGPR and PR.

The clinical sensitivity and specificity based on "Progression" and "No-progression" are summarized in the following table.

		Clinical Assessment		
		Progression	No Progression	Total
Change in Sebia FLC	PD*	28	6	34
	No-PD**	13	504	517
	Total	41	510	551
Clinical Sensitivity: 68.3% (28/41) (95% CI: 54.0%- 82.5%) Clinical Specificity: 98.8% (504/510) (95% CI: 97.9%- 99.8%)				

*Progression: include samples defined as 'Progressive Disease'.
**No Progression: include samples as 'Good Response, Moderate Response, and Stable Disease'.

Monitoring of AL Amyloidosis

1. Clinical Sensitivity and Clinical Specificity

The clinical performance of the FLC Kappa and FLC Lambda assays as an aid in monitoring of AL-Amyloidosis patients was evaluated in serum samples from subjects diagnosed with AL-Amyloidosis. The patient inclusion and exclusion criteria were as follows:

Inclusion criteria:

- ≥ 18 years of age
- confirmed diagnosis of AL-Amyloidosis at baseline time point
- Adequate sample volume for testing
- Samples from patients with 1 baseline time point and at least 2 follow-up time points
- signed informed consent.
- Less than 5 freeze thaw cycles
- Frozen samples (storage at -18/-30°C or -70/-80°C)
- The following information are needed for each sample:
  Age, sex, race, ethnicity of patient
  Time interval between 2 time points

Treatment start/change date(s), use of chemotherapy or radiation treatment or bone marrow transplant (when available)
Serum Protein Electrophoresis (SPEP) (M-spike)
Serum IFE

- At least 20 samples with a "progressive" response criterion, and a significative representation of all the other responses criteria

Exclusion criteria:

- patients with less than 2 follow-up points.
- Not enough information available collected to define the status of the patient, based on the selected guidance to perform the classification
- Missing FLC values at collection or at retest with the predicate or the candidate

Of the 87 AL-Amyloidosis subjects, 13 subjects were diagnosed with IgG Kappa, 26 IgG Lambda, 1 IgA Kappa, 6 IgA Lambda, 4 IgM Lambda, 2 Light Chain Kappa AL-Amyloidosis and 14 Light Chain Lambda AL-Amyloidosis. Three of the 87 AL-Amyloidosis subjects had two subtypes (clones) as follows: 1 IgG Kappa and IgD Lambda; 1 IgG Lambda and IgG Lambda; and 1 IgG Kappa and IgM Kappa.

Among 87 subjects, 53 (61%) were male and 34 (39%) were female. The median age was 62 years old with the age ranging from 40 to 81 years old. Most of the subjects were Caucasians (n=75; 86.2%). The remaining subjects were: African American (n=8; 9.2%,), and Unknown (n=4; 4.6%). A total of 190 follow-up samples were tested by the Sebia Kappa FLC and Lambda FLC Assays. The duration of the monitoring days ranged from 64 days to 4474 days (with a median of 445 days).

To evaluate the clinical performance of Sebia FLC Kappa and FLC Lambda assay, the response criteria for each follow-up sample of each patient was compared to the respective individual clinical status. Five response criteria: CR (Complete Response), VGPR (Very Good Partial Response), PR (Partial Response), SD/NR (Stable Disease/No response), PD (Progressive Disease) were used to categorize each monitoring outcome for each patient based on the FLC Kappa and FLC Lambda results according to the following two therapy response evaluation criteria:

- **Evaluation Mode 1** based on criteria established by Palladini and colleagues (Comenzo et al., 2012; Palladini et al., 2012; Palladini et al., 2021),

- **Evaluation Mode 2** based on National Comprehensive Cancer Network. "NCCN clinical practice guidelines in oncology (NCCN guidelines)." Systemic Light Chain Amyloidosis Version 1 (2022): 1–27

The response criteria based on above Modes are summarized in the table below:

Response Criteria	Serum M Protein/ IFE	Evaluation Mode 1	Evaluation Mode 2
CR	Serum and urine IFE negative	FLC levels and ratio normal	FLC levels and ratio normal
VGPR		Reduction in the dFLC to <40 mg/L	Reduction in the dFLC to <40 mg/L
PR		dFLC > 50 mg/L 1. A greater than 50% reduction in the initial dFLC value 2. For patients with an initial dFLC value of less than 50 mg/L a low FLC response is indicated if dFLC < 10 mg/L	dFLC > 50 mg/L A greater than 50% reduction in the initial dFLC value
SD = NR		Less than a PR	Less than a PR
PD	From CR, any detectable monoclonal protein From PR, 50% increase in serum M protein to >0.5g/dL or 50% increase in urine M protein to >200 mg/dL	From CR, abnormal FLC ratio (light chain must at least double) From PR, Serum FLC increase of ≥ 50% to dFLC > 50 mg/L	From CR, abnormal FLC ratio (light chain must at least double) From PR, Serum FLC increase of ≥ 50% to iFLC > 100 mg/L

- iFLC = involved FLC (monoclonal chain)
- dFLC = iFLC – niFLC (not involved FLC)

For each of 190 monitoring observations, the results of Sebia Kappa and Lambda FLC assay in combination with other laboratory results were used to assign a response category and compared to the clinical assessment. The results are summarized in the following tables:

Evaluation Mode 1:

Response based on Sebia FLC	Clinical Assessment					
	CR	**VGPR**	**PR**	**SD**	**PD**	**Total**
CR	17	2	2	0	1	22
VGPR	4	74	14	14	2	108
PR	1	2	9	1	2	15
SD	0	2	4	20	2	28
PD	0	2	0	0	15	17
Total	22	82	29	35	22	190
Concordance (n/N) (95% CI)	77.3% (17/22) (59.8%; 94.8%)	90.2% (74/82) (83.8%; 96.7%)	31.0% (9/29) (14.2%; 47.9%)	57.1% (20/35) (40.7%; 73.5%)	68.2% (15/22) (48.7%; 87.6%)	71.1% (135/190) (64.6%; 77.5%)

The clinical sensitivity and specificity based on "Progression" and "No-progression" are summarized in the following table.

Evaluation Mode 1:

		Clinical Assessment		
		Progression	**No Progression**	**Total**
Response based on Sebia FLC	**PD***	15	2	17
	No-PD**	7	166	173
	Total	22	168	190
Clinical Sensitivity: 68.2% (15/22) (95% CI: 48.7% to 87.6%) Clinical Specificity: 98.8% (166/168) (95% CI: 97.2% to 100.0%)				

*Progression: include samples defined as 'Progressive Disease'.

**No Progression: include samples as 'Complete Response, Very Good Partial Response, Partial Response, and Stable Disease'.

Evaluation Mode 2:

Response based on Sebia FLC	**Clinical Assessment**					
	CR	**VGPR**	**PR**	**SD**	**PD**	**Total**
CR	6	8	2	0	0	16
VGPR	9	73	14	15	3	114
PR	0	3	9	1	2	15
SD	0	2	4	20	2	28
PD	0	2	0	0	15	17
Total	15	88	29	36	22	190
Concordance (n/N) (95% CI)	40.0% (6/15) (15.2%; 64.8%)	83.0% (73/88) (75.1%; 90.8%)	31.0% (9/29) (14.2%; 47.9%)	55.6% (20/36) (39.3%; 71.8%)	68.2% (15/22) (48.7%; 87.6%)	64.7% (123/190) (57.9%; 71.5%)

The clinical sensitivity and specificity based on "Progression" and "No-progression" are summarized in the following table.

Evaluation Mode 2:

		Clinical Assessment		
		Progression	**No Progression**	**Total**
Response based on Sebia FLC	**PD***	15	2	17
	No-PD**	7	166	173
	Total	22	168	190
Clinical Sensitivity: 68.2% (15/22) (95% CI: 48.7% to 87.6%) Clinical Specificity: 98.8% (166/168) (95% CI: 97.2% to 100.0%)				

*Progression: include samples defined as 'Progressive Disease'.

**No Progression: include samples as 'Complete Response, Very Good Partial Response, Partial Response, and Stable Disease'.

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Refer to K210623

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.