

## 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION

### DECISION SUMMARY

**A. 510(k) Number:**

k113823

**B. Purpose for Submission:**

New device

**C. Measurand:**

Immunoglobulin IgM Kappa (combined  $\mu$  heavy and  $\kappa$  light chain) and  
Immunoglobulin IgM Lambda (combined  $\mu$  heavy and  $\lambda$  light chain)

**D. Type of Test:**

Quantitative and Semi-Quantitative, Nephelometry

**E. Applicant:**

The Binding Site Group, Ltd.

**F. Proprietary and Established Names:**

Hevylite™ Human IgM Kappa Kit for use on Siemens BN™ II Systems  
Hevylite™ Human IgM Lambda Kit for use on Siemens BN™ II Systems

**G. Regulatory Information:**

1. Regulation section:

21 CFR § 866.5510, Immunoglobulins A, G, M, D, and E Immunological Test System

2. Classification:

Class II

3. Product codes:

CFN - Method, Nephelometric, Immunoglobulins (G, A, M)  
PDE – Immunoglobulin M kappa heavy and light chain combined  
PDF – Immunoglobulin M lambda heavy and light chain combined

4. Panel:

Immunology 82

**H. Intended Use:**

1. Intended use(s):

Hevylite Human IgM Lambda Kit for use on Siemens BN™II is intended for the in vitro quantification of IgM Lambda (combined  $\mu$  heavy and  $\lambda$  light chain) concentration in human serum on the Siemens Behring Nephelometer™ II (BN™ II). The test result is to be used with previously diagnosed Waldenstrom's macroglobulinemia in conjunction with other clinical and laboratory findings.

This assay has not been established for the diagnosis, monitoring and prognosis of Waldenstrom's macroglobulinemia.

Hevylite Human IgM Kappa Kit for use on Siemens BN™II is intended for the in vitro quantification of IgM Kappa (combined  $\mu$  heavy and  $\kappa$  light chain) concentration in human serum on the Siemens Behring Nephelometer™ II (BN™ II). The test result is to be used with previously diagnosed Waldenstrom's macroglobulinemia in conjunction with other clinical and laboratory findings.

This assay has not been established for the diagnosis, monitoring and prognosis of Waldenstrom's macroglobulinemia.

2. Indication(s) for use:

Same as intended use.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

Siemens Behring Nephelometer™ II (BN™ II) (k943997)

**I. Device Description:**

The Hevylite™ Human IgM Kappa Kit and IgM Lambda Kit contain polystyrene latex coated with polyclonal monospecific sheep anti-human IgM antibody against combined  $\mu$  heavy and  $\kappa$  light chain or combined  $\mu$  heavy and  $\lambda$  light chain, a single level calibrator, two controls (low and high) and supplementary reagent in liquid form. The reagents contain 0.099% sodium azide as preservative.

**J. Substantial Equivalence Information:**

1. Predicate device name(s) and 510(k) number(s)

Sebia's Hydrasys Agarose Gel Electrophoresis Apparatus/Hydrigel 15, 30 Protein Kit, SPE (k960029)

Sebia's Hydrigel Immunofixation, 6 IF, 12 IF PENTA Kits/ Hydrigel IF, Double IF, 2 IF, & 4 IF Kits (k960669)

Hevylite™ Human IgA Kappa Kit for use on Siemens BN™ II Systems and Hevylite™

Human IgA Lambda Kit for use on Siemens BN™ II Systems (k082823)

Siemens N Antisera to Human Immunoglobulins (IgG, IgA, and IgM) and N/T Protein Control LC (k083445)

2. Comparison with predicate:

Similarities/Differences		
Item	New Device	Predicates
	Hevylite IgM Kappa and IgM Lambda kit	Hevylite IgA Kappa kit and IgA Lambda kit (k082823)
Intended Use	Quantification of IgM $\kappa$ (combined $\mu$ heavy and $\lambda$ light chain) or IgM $\lambda$ (combined $\mu$ heavy and $\lambda$ light chain) concentration in human serum on the Siemens BN <sup>TM</sup> II	Quantification of IgA $\kappa$ (combined $\alpha$ heavy and $\kappa$ light chain) or IgA $\lambda$ (combined $\alpha$ heavy and $\lambda$ light chain) in human serum on the Siemens BN II
Indications for Use	Used with previously diagnosed Waldenstrom's macroglobulinemia and in conjunction with other clinical and laboratory findings.	Used in previously diagnosed IgA multiple myeloma
Sample Matrix	Serum	Same
Detection Method	Nephelometric	Same
Instrument	BN <sup>TM</sup> II	Same
Measuring range	<p>IgM <math>\kappa</math>: 0.2 – 6.4 g/L            IgM <math>\lambda</math>: 0.175 – 5.60 g/L            (at standard 1/100 dilution)</p> <p>Extended Range for IgM <math>\kappa</math>:            1/5 dilution: 0.01 – 0.32 g/L            1/20 dilution: 0.04 – 1.28 g/L            1/100 dilution: 0.2 – 6.4 g/L            1/400 dilution: 0.8 – 25.6 g/L            1/2000 dilution: 4 – 128 g/L</p> <p>Extended Range for IgM <math>\lambda</math>:            1/5 dilution: 0.009 – 0.280 g/L            1/20 dilution: 0.035 – 1.12 g/L            1/100 dilution: 0.175 – 5.60 g/L            1/400 dilution: 0.7 – 22.4 g/L            1/2000 dilution: 3.5 – 112 g/L</p>	<p>IgA <math>\kappa</math>: 0.35 – 11.2 g/L            IgA <math>\lambda</math>: 0.33 – 10.4 g/L            (at standard 1/100 dilution)</p>
Reference Range	<p>IgM <math>\kappa</math>: 0.29 - 1.82 g/L            IgM <math>\lambda</math>: 0.17 - 0.94 g/L            IgM <math>\kappa/\lambda</math> ratio: 0.96 - 2.3</p>	<p>IgA <math>\kappa</math>: 0.48 – 2.82 g/L            IgA <math>\lambda</math>: 0.36 – 1.98 g/L            IgA <math>\kappa/\lambda</math> Ratio: 0.80 – 2.04</p>
Controls	One low and one high control (serum, ready to use)	Same
Calibrator	Binding Site Hevylite Calibrator <sup>TM</sup>	Binding Site Hevylite Calibrator <sup>TM</sup>
Antisera specificity	polyclonal monospecific sheep antibody (anti-human IgM combined $\mu$ heavy and $\kappa$ light chain or combined $\mu$ heavy and $\lambda$ light chain antiserum) coated onto polystyrene latex	Sheep anti-human IgA combined $\alpha$ heavy and $\kappa$ light chain or combined $\alpha$ heavy and $\lambda$ light chain antiserum
Result	Quantitative measurement by nephelometry	Same

Similarities/Differences				
Item	New Device	Predicate		
	Hevylite IgM Kappa and IgM Lamda kit	Serum Protein Electrophoresis (SPE) (k960029)	Siemens Total Ig (k083445)	Immunofixation Electrophoresis (IFE) (k960669)
Intended Use	Quantification of IgM $\kappa$ (combined $\mu$ heavy and $\lambda$ light chain) or IgM $\lambda$ (combined $\mu$ heavy and $\lambda$ light chain) concentration in human serum on the Siemens BN™ II	Protein separation to assess for protein pattern abnormalities in serum and urine	Quantitative determination of immunoglobulins (IgG, IgA and IgM) in human serum, heparinized and EDTA plasma, human urine and cerebrospinal fluid (CSF) by means of immunonephelometry on the BN systems.	Identification of monoclonal immunoglobulins (IgG, IgA, or IgM Heavy Chain) and light chains (Kappa or Lambda Light Chain) in human serum and urine using the Hydrasys system
Indications for Use	Used with previously diagnosed Waldenstrom's macroglobulinemia and in conjunction with other clinical and laboratory findings.			Aid in the diagnosis of monoclonal gammopathies
Sample Matrix	Serum	Serum and urine	Serum, heparinized or EDTA plasma, urine and CSF	Serum and urine
Detection Method	Nephelometric	Electrophoresis	Nephelometric	Immunofixation electrophoresis
Instrument	BN™II	Sebia Hydrasys System	BN ProSpec®	Sebia Hydrasys System
Measuring range	IgM $\kappa$ : 0.2 -6.4 g/L IgM $\lambda$ : 0.175 - 5.60 g/L (at standard 1/100 dilution)	Minimum detection ~ 21-44 mg/dL monoclonal protein	IgM : 0.168 - 5.37 g/L (at standard 1/20 dilution)	Not applicable; Qualitative
Reference Range	IgM $\kappa$ : 0.29 - 1.82 g/L IgM $\lambda$ : 0.17 - 0.94 g/L IgM $\kappa/\lambda$ ratio: 0.96 - 2.3	Absence of monoclonal proteins	0.4 - 2.3 g/L	Absence of monoclonal immunoglobulins
Controls	One low and one high control (serum, ready to use)	Sebia (PN4785) Control Serum	Protein Controls N Protein (serum)	Not applicable
Calibrator	Binding Site Hevylite Calibrator™	Not applicable	N Protein Standard (serum)	Not applicable
Antisera specificity	polyclonal monospecific sheep antibody (anti-human IgM combined $\mu$ heavy and $\kappa$ light	No antisera required	Rabbit anti-human immunoglobulins	Mammalian immunoglobulins anti-human alpha, gamma, and mu heavy chains, anti-

Similarities/Differences				
Item	New Device	Predicate		
	Heavylite IgM Kappa and IgM Lamda kit	Serum Protein Electrophoresis (SPE) (k960029)	Siemens Total Ig (k083445)	Immunofixation Electrophoresis (IFE) (k960669)
	chain or combined $\mu$ heavy and $\lambda$ light chain antiserum) coated onto polystyrene latex			human $\kappa$ light chains and anti-human $\lambda$ light chains
Result	Quantitative measurement by nephelometry	Semi-quantitative results are calculated from Total Protein for each of five protein fractions (albumin, $\alpha$ -1 AT, $\alpha$ -2 beta globulin, $\gamma$ globulin)  Qualitative results are visual interpretation of densitometric scan of each five protein fractions according to pattern symmetry by pathologist	Quantitative measurement by nephelometry	Qualitative visual interpretation of each of 6 electrophoretic mobility bands: (Total Protein, IgG IgA, IgM, $\kappa$ and $\lambda$ bands) by pathologist whether it is restricted monoclonal band or homogeneous polyclonal band

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

CLSI EP-5A: Evaluation of Precision Performance of Clinical Chemistry.

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP-17A: Determination of Limits of Detection and Limits of Quantitation.

C28-A3: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory

EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition

**L. Test Principle:**

Evaluating the concentration of a soluble antigen by nephelometry involves the addition of the test sample (with either IgM Kappa (IgM $\kappa$ ) or IgM Lambda (IgM $\lambda$ )) to a solution containing the appropriate antibody (anti-IgM $\kappa$  or anti-IgM $\lambda$ ) in a reaction vessel or cuvette. A beam of light is passed through the cuvette and as the antigen-antibody reaction proceeds,

the light passing through the cuvette is scattered increasingly as insoluble immune complexes are formed. The antibody in the cuvette is in excess so the amount of immune complex formed is proportional to the antigen concentration. In nephelometry, the light scatter is monitored by measuring the light intensity at an angle away from incident light. A series of calibrators of known antigen concentration are assayed initially to produce a calibration curve of measured light scatter versus antigen concentration. Samples of unknown antigen concentration can then be assayed and the results read from the calibration curve.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

A precision study was conducted in accordance with CLSI document EP05-A2. The study was carried out by testing three serum sample pools with different concentrations of IgM $\kappa$  or IgM $\lambda$  that span the measuring range of the assays at the recommended 1/100 dilution (0.2–6.4 g/L and 1.75–5.60 g/L respectively). An additional study was performed to evaluate the five instrument dilutions. All samples were analyzed using three different reagent lots on one analyzer. The study was performed over 21 working days, with 2 runs per day and each sample run in duplicate. A total of 84 measurements per sample were tested. Results are summarized below:

Hevylite™ Human IgM Kappa Kit for use on Siemens BN™ II Systems

IgMK Sample	Mean g/L	Within-Run		Between-Run		Between-Day		Between-lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	0.352	0.0191	5.6%	0.0114	3.3%	0.145	4.2%	0.015	4.25%	0.0266	7.7%
Medium	1.162	0.0359	3.2%	0.0324	2.9%	0.534	4.8%	0.044	3.77%	0.0721	6.5%
High	4.854	0.1456	2.8%	0.1388	2.7%	0.2183	4.2%	0.126	2.6%	0.2969	5.7%

Hevylite™ Human IgM Lambda Kit for use on Siemens BN™ II Systems

IgML Sample	Mean g/L	Within-Run		Between-Run		Between-Day		Between-lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	0.303	0.0098	3.5%	0.0070	2.5%	0.0150	5.4%	0.015	4.99%	0.0193	6.9%
Medium	0.767	0.0115	1.7%	0.0075	1.1%	0.0563	8.5%	0.066	8.59%	0.0579	8.7%
High	4.240	0.1694	4.2%	0.1140	2.8%	0.3743	9.3%	0.344	8.1%	0.4264	10.6%

b. *Linearity/assay reportable range:*

A linearity study based on CLSI document EP-6-A, was carried out. Linearity across the assay ranges of IgM $\kappa$  (0.2 – 6.4 g/L) and IgM $\lambda$  (0.175 – 5.6 g/L) at the recommended 1/100 dilution was evaluated by testing each with a high and low dilution pool series. The high pools were prepared from serum spiked with polyclonal IgM protein and the low pools were prepared from serum diluted with instrument diluent. The pooled IgM $\kappa$  sera had a high concentration of 6.437 g/L and a low concentration of 0.183 g/L. The pooled IgM $\lambda$  sera had a high concentration of 5.683 g/L and a low concentration of 0.171 g/L. A dilution series of 11 analyte levels was prepared by blending the high pool and the low pool. All testing was done in triplicate. The % recovery was calculated as the differences of expected values and

the observed values. The % recovery ranged from 80 to 120% at each concentration. The observed values were graphed against the calculated values and a linear regression was performed. The regression plot equations where y is the measured level of IgM $\kappa$  or  $\lambda$  concentration and x the theoretical concentration were:

$$y = 1.035x - 0.075 \text{ (g/L), } r^2 = 0.9939 \text{ for IgM}\kappa$$

$$y = 1.065x - 0.2175 \text{ (g/L), } r^2 = 0.9941 \text{ for IgM}\lambda$$

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability:

The calibrator, the internal reference standard (IR) and controls are traceable to ERM-DA470k International Reference Material. The IR is prepared from pooled human sera and is used to control calibration between lots.

Device Stability:

Real-time stability studies were performed to support the following stability claims of the Hevylite IgM Kappa and Hevylite IgM Lambda kits:

- Shelf-life stability of the opened kits are stable up to 2 months after opening when stored at 2–8°C.
- Shelf-life stability for unopened kits when stored at 2 – 8°C is 12 months.

Sample Stability:

Sample stability studies were conducted. Fresh serum samples can be used when stored at 2 – 8°C for up to 21 days. Frozen serum samples can be used when stored at -20°C for up to a year.

d. *Detection limit:*

The limit of blank (LoB) and limit of detection (LoD) studies were performed following the protocol in CLSI EP-17A. The detection limit was determined by testing a blank sample (instrument diluent; LoB), the lowest calibrator (LoQ), and a sample with value close to the blank (LoD) sample at a neat sample dilution (1/1).

The LoB was determined by running diluent alone. The assigned concentrations were equivalent to 0.006 g/L for IgM $\kappa$  and 0.000 g/L for IgM $\lambda$  at minimum sample dilution (1/5). Samples were tested 60 times for LoB.

The LoQ samples were the bottom calibrator diluted in instrument diluent. The assigned concentrations were equivalent to 0.011 g/L for IgM $\kappa$  and 0.008 g/L for IgM $\lambda$  at minimum sample dilution (1/5). Samples were tested 40 times for LoQ.

The LoD is the lowest measurable concentration of the analyte that can be distinguished from zero; it has been calculated as 0.0095 g/L for IgM $\kappa$  and 0.003 for IgM $\lambda$  for the minimum sample dilution for the assay (1/5). Samples were tested 60 times for LoD.

e. *Analytical specificity:*

Interfering Substances:

Interference by endogenous substances were evaluated by addition of hemoglobin (5g/L), bilirubin (200 mg/L) and chyle (1500 FTU) to test serum samples representing analyte concentrations at the lower end of the reference range, the upper end of the reference range, as well as a pathological concentration. The negative control pools were prepared by spiking commercially obtained blank into the sera base pools. Samples were tested a minimum of three times each. No significant interference was observed with the interferents tested. Rheumatoid factor was not evaluated.

#### Hevylite™ Human IgM Kappa Kit for use on Siemens BN™ II Systems

IgMκ Sample	Analyte Level (g/L)	Hemoglobin		Bilirubin		Chyle	
		Spiked Concentration (g/L)	No. of Replicates	Spiked Concentration (mg/L)	No. of Replicates	Spiked Concentration (FTU)	No. of Replicates
bottom of normal range	0.29	5	3	200	3	1500	3
top of normal range	1.82	5	4	200	4	1500	4
pathological	5.88	5	4	200	4	1500	4

#### Hevylite™ Human IgM Lambda Kit for use on Siemens BN™ II Systems

IgMλ Sample	Analyte Level (g/L)	Hemoglobin		Bilirubin		Chyle	
		Spiked Concentration (g/L)	No. of Replicates	Spiked Concentration (mg/L)	No. of Replicates	Spiked Concentration (FTU)	No. of Replicates
bottom of normal range	0.17	5	3	200	3	1500	3
top of normal range	0.94	5	4	200	4	1500	4
pathological	5.12	5	4	200	4	1500	4

An additional endogenous interferant study was performed with a known IgMκ (0.74 g/L at a minimum 1/5 sample dilution) and a known IgMλ (0.052 g/L at a minimum 1/5 sample dilution) processed serum sample prepared from diluted calibrators and tested in triplicate with the following interferents: 4.56 g/L hemoglobin, 199.6 mg/L bilirubin, 1309 FTU of chyle. Minimal interference by these substances were observed (-2.2%; 4.8%; -8.3% on IgMκ and 4.5%; 1.9%; -9.88% on IgMλ respectively).

The package insert states in the Limitations section that “Nephelometric assays are not suitable for measurement of highly lipemic or hemolyzed samples, or samples containing high levels of circulating immune complexes due to the unpredictable degree of non-specific scatter these sample types might generate. Unexpected results should be confirmed using alternative assay method”.

#### Cross reactivity:

Cross reactivity studies were carried out by testing Hevylite IgM Kappa and Hevylite IgM Lambda assays in the presence of high concentrations of potentially cross-reacting monoclonal proteins in samples from IgAκ, IgAλ, IgGκ, IgGλ, κ light chain and λ light chain multiple myeloma patient sera. No significant cross reactivity was observed.

The potential cross reacting substances were tested at the following levels:

Substance	Highest Level Tested (g/L)
IgA $\kappa$	39.6
IgA $\lambda$	47.1
IgG $\kappa$	58.5
IgG $\lambda$	45.5
$\kappa$ Light chain	6.5
$\lambda$ Light chain	8.4

The samples were all tested for total IgG, total IgA, total IgM and also with the Hevylite IgM Kappa and IgM Lambda assays. The results for total IgM were compared with the results obtained by the Hevylite IgM Kappa and IgM Lambda assays.

In addition IgM $\kappa$  Waldenstrom's macroglobulinemia patient samples (highest 41.5 g/L) were tested on Hevylite IgM lambda kits to investigate potential cross-reactivity, and similarly IgM $\lambda$  Waldenstrom's macroglobulinemia patient samples (highest 48.5 g/L) were tested on IgM kappa kits.

Antigen excess effect:

The possibility of antigen excess occurring when using the devices on BN II Nephelometer was evaluated with three batches of patient serum samples containing high levels of IgM $\kappa$  and IgM $\lambda$  monoclonal protein concentrations above the assay range. No antigen excess effect up to 100 g/L of IgM $\kappa$  and 100 g/L IgM $\lambda$  were observed at the standard 1/100 sample dilution.

*f. Assay cut-off:*

The cut off values are the reference ranges for the normal population which have been established from the reference range study.

2. Comparison studies:

*a. Method comparison with predicate device:*

Analyses of the method comparisons were performed with each of the three predicate devices: Total IgM, SPE and IFE.

Comparison with Total IgM quantitative measurement (k083445):

Testing was performed on 110 normal adult sera and 78 IgM Waldenstrom's macroglobulinemia (48 IgM $\kappa$  and 30 IgM $\lambda$ ) samples.

The table below shows the comparison of 186 sera tested by Dade Behring Total IgM and Hevylite IgM Kappa and IgM Lambda with exclusion of two outlier samples.

A limitation of the Hevylite IgM Kappa and IgM Lambda device is that samples from patients with hyperviscosity syndrome or cryoglobulinemia may not report accurately.

Regression analysis (Passing Bablok) of these samples is summarized below:

Regression equation	n	95% CI of Slope	95% CI of Intercept	R <sup>2</sup>
Y = 1.16x - 0.32g/L	186	1.10 to 1.22	-0.40 to -0.23	0.94

Comparison with SPE semi-quantitative measurement (k960029):

110 normal and 78 IgM Waldenstrom's macroglobulinemia presenting samples were compared by Sebia SPE semi-quantitative measurement and Binding Site Hevylite IgM Kappa and IgM Lambda quantitative devices.

Samples outside the 95% reference ranges for IgMκ, IgMλ or IgMκ/IgMλ ratio for the Hevylite were classified as abnormal/positive and samples within the reference range were considered normal/negative. For the SPE assay, samples with quantifiable monoclonal protein were considered abnormal/positive and samples without detectable monoclonal protein were classified as normal/negative. Results are shown in table below:

		Sebia SPE		
		Positive/ Abnormal	Negative/ Normal	Total
Hevylite Assay	Positive/Abnormal	74	4	78
	Negative/Normal	0	110	110
	Total	74	114	188

Positive Percent Agreement: 100% (74/74) (95% CI: 100% – 100%)

Negative Percent Agreement: 96.5 % (110/114) (95% CI: 93.1% – 99.9 %)

Overall Percent Agreement: 97.9% (184/188) (95% CI: 95.9% – 100%)

Comparison by IFE (k960669):

Only 60 of the 78 IgM Waldenstrom's macroglobulinemia samples had IFE analysis. A positive IFE result and an abnormal Hevylite result were obtained for all of the 60 clinical samples tested.

*b. Matrix comparison:*

Not applicable.

3. Clinical studies:

*a. Clinical Sensitivity and specificity:*

Not applicable.

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

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Adult normal range was assessed on a total 120 sera samples from healthy UK adult blood donors. The assays were performed on the Dade Behring BN II™ analyser. A non-parametric analysis of specimens for the distribution of IgMκ and IgMλ was performed.

Normal Adult Serum	Mean	Median	95 <sup>th</sup> percentile range
IgM $\kappa$ (g/L)	0.72	0.63	0.29 – 1.82 g/L
IgM $\lambda$ (g/L)	0.45	0.42	0.17 – 0.94 g/L
IgM $\kappa$ /IgM $\lambda$ ratio	1.59	1.59	0.96 – 2.30 g/L

The upper and lower limits of the reference range for IgM $\kappa$  (0.29 – 1.82 g/L), IgM $\lambda$  (0.17 – 0.94 g/L) and the IgM $\kappa$ / $\lambda$  ratio (0.96 – 2.30) are defined as the “cut-offs”. Samples with a Hevylite result above any of these reference ranges are classified as positive i.e. abnormal.

The cut-offs have been validated by comparing percentage agreement in detection of monoclonal protein by SPE vs. Hevylite IgM Kappa and IgM Lambda and kappa/lambda ratio abnormal results

**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.