510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k042939

B. Purpose for Submission:
New Device

C. Measurand:
Monoclonal Immunoglobulins (IgG, IgA, IgM, Kappa, Lambda) in serum

D. Type of Test:
Capillary Zone Electrophoresis

E. Applicant:
SEBIA, INC.

F. Proprietary and Established Names:
CAPILLARYS IMMUNOTYPING, PN 2100

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.5510 Immunoglobulins (A, G, M, D, E) Immunological test system
   21 CFR 866.5550 Immunoglobulin (light chain specific) immunological test system
   21 CFR 862.1630 Electrophoretic, Protein Fractionation
2. Classification:
   II
3. Product codes:
   CFF - Immunoelectrophoretic, Immunoglobulins (G, A, M)
   DFH – Kappa, Antigen, Antiserum, Control
   DEH – Lambda, Antigen, Antiserum, Control
   CEF – Electrophoretic, Protein Fractionation
4. Panel:
   Immunology 82
   Clinical Chemistry 75

H. Intended Use:

1. Intended use(s):
   The CAPILLARYS IMMUNOTYPING kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human serum with the CAPILLARYS System, SEBIA, for capillary electrophoresis. It is used in conjunction with the CAPILLARYS PROTEIN (E) 6 or CAPILLARYS ß1-ß2^{+} kits, SEBIA, designed for serum proteins separation into 6 major fractions in alkaline buffer (pH 9.9).

   The CAPILLARYS performs all procedural sequences automatically to obtain a protein profile for qualitative analysis. Each sample is mixed with individual antisera that are specific against gamma (Ig G), alpha (Ig A) and mu (Ig M) heavy chains, and kappa (free and bound) light chains and lambda (free and bound) light chains, respectively.

   The protein fractions, separated in silica capillaries, are directly detected by their absorbance at 200 nm. The electrophoregrams are evaluated visually to detect the presence of specific

reactions with the suspect monoclonal proteins.
For *in vitro* diagnostic use only.

2. Indication(s) for use:
   The CAPILLARYS IMMUNOTYPING kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human serum with the SEBIA CAPILLARYS System, for capillary electrophoresis. It is used in conjunction with the CAPILLARYS PROTEIN (E) 6 or CAPILLARYS ß1-ß2^{+} kits, designed for serum proteins separation into 6 major fractions in alkaline buffer (pH 9.9).

   The CAPILLARYS system performs all procedural sequences automatically to obtain a protein profile for qualitative analysis. Each sample is mixed with individual antisera that are specific against gamma (Ig G), alpha (Ig A) and mu (Ig M) heavy chains, and kappa (free and bound) light chains and lambda (free and bound) light chains.

   The protein fractions, separated in silica capillaries, are directly detected by their absorbance at 200 nm. The electrophoregrams are evaluated visually by comparing the profile of the untreated sample with the individual profiles treated with the respective antisera. Monoclonal immunoglobulins are thus detected and identified.

   Identification of Monoclonal immunoglobulins is essential for the classification of monoclonal gammopathies by the class and type of involved immunoglobulins.
   For *in vitro* diagnostic use only.

3. Special conditions for use statement(s):
   The device is for prescription use only.
4. Special instrument requirements:
   This device has been validated for use with the SEBIA CAPILLARYS System (capillary electrophoresis).

I. Device Description:

The CAPILLARYS IMMUNOTYPING (PN 2100) kit is designed for optimal performance on the SEBIA CAPILLARYS System (PN 1220), an automated capillary electrophoresis system (K022227 cleared on July 13, 2002).

The CAPILLARYS IMMUNOTYPING (PN 2100) kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human serum and the kit contains 60 Immunotyping antisera segments which are ready to use. Each segment is intended to run one sample. The antisera segments have antibodies specific against gamma (IgG), alpha (IgA), mu (IgM) heavy chains and kappa and lambda (free and bound) light chains.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Sebia Hydragel Immunofixation Kit
2. Predicate 510(k) number(s):
   k960669
3. Comparison with predicate:

Similarities		
Item	New Device	Predicate Device
IFE Antisera Specificity	Antibody specificity to heavy chains (IgG, IgA, IgM) and to light chains (kappa, lambda).	Same
IFE Antisera Storage	2 – 8 ºC or room temperature (15 – 30 ºC)	Same
Results	Qualitative Interpretation	Same

Differences		
Item	Device	Predicate
Intended use/ Indication for use	The CAPILLARYS IMMUNOTYPING kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human serum with the SEBIA CAPILLARYS System, for capillary electrophoresis.	The HYDRAGEL IF, 6 IF, 12 IF Penta kits/Hydragel IF kits are designed for the detection of monoclonal proteins in human serum and urine by Immunofixation electrophoresis. The kits are used in conjunction with the semi-automated HYDRASYS electrophoresis apparatus.
Technology	SIFE/s: Capillary Electrophoretic Migration with Immunofixation by Subtraction (Immunotyping).	SIFE: Agarose gel Electrophoretic Migration with Immunofixation.
Methodology	Capillary Electrophoresis	Gel Electrophoresis
Equipment	Automated CAPILLARYS electrophoresis System	Semi-automated HYDRASYS electrophoresis apparatus
Sample type	Serum	Serum and urine
Sample size	240 µL	100 µL
Buffer pH	pH 9.9	pH 9.1
Interferences	Serum: Hemolyzed, lipemic samples. Fibrinogen.	Serum: Hemolyzed and turbid/viscous samples. Fibrinogen. Cryoglobulin, cryogel. Urine: Boric acid and other acid preservative.
Lowest detectible Limit	25 mg/dL	12-25 mg/dL

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

None provided.

L. Test Principle:

The CAPILLARYS System uses the principle of capillary electrophoresis in free solution. With this technique, charged molecules are separated by their electrophoretic mobility in an alkaline buffer with a specific pH. Separation also occurs according to the electrolyte pH and electroosmotic flow.

CAPILLARYS IMMUNOTYPING is performed with specific antibodies to identify abnormal proteins in the beta globulin and gamma globulin fraction zones of the serum protein electrophoregrams. Abnormal serum fractions in these zones are always suspect of being monoclonal proteins (M-proteins, paraproteins, monoclonal immunoglobulins) and therefore, an indication of monoclonal gammopathies.

The CAPILLARYS System has 8 capillaries functioning in parallel. In this system, a sample dilution is prepared and injected simultaneously by aspiration at the anodic end of six capillaries (capillaries No. 7 and 8 are not used). The reference (ELP) pattern is obtained by injection of the sample mixed with ELP solution in capillary No. 1 providing a complete electrophoretic pattern of the sample's proteins. The antisera patterns are obtained by injection in capillaries No. 2 to 6 of the previously diluted samples mixed with specific antisera against gamma (Ig G), alpha (Ig A), mu (Ig M) heavy chains, and against free and bound kappa and lambda light chains.

A high voltage protein separation is then performed and direct detection of the proteins is made at 200 nm at the cathodic end of the capillary. The capillaries are immediately washed with a Wash Solution and prepared for the next analysis with buffer.

In CAPILLARYS IMMUNOTYPING, proteins are detected in the following order from cathode to anode: gamma globulins, beta-2 globulins, beta-1 globulins, alpha-2 globulins, alpha-1 globulins and albumin with each zone containing one or more proteins. The antigen - antibody complex (between the sample immunoglobulins and the specific antiserum) has a very anodic mobility (between alpha-1 zone and albumin or more anodic than albumin).

The superimposition of the antisera patterns with the reference pattern (ELP) permits to visualize the disappearance and / or the decrease of a monoclonal fraction on the antiserum pattern and to indicate a gammopathy.

The immunotyping is performed in three automated steps:

1. The sample dilution is prepared with specific diluent which is preloaded in the antisera segment. This dilution is selected by the user of the CAPILLARYS system according to the sample's immunoglobulins concentration.

« HYPERGAMMA » if total immunoglobulins level is > 2 g/dL (hypergammaglobulinemia),
« HYPOGAMMA » if total immunoglobulins level is < 0.8 g/dL (hypogammaglobulinemia),
« STANDARD » if total immunoglobulins level is comprised between 0.8 and 2 g/dL (dilution program by default).

2. The diluted serum sample is then mixed with individual specific antisera. The antigen - antibody complex is formed rapidly in the liquid medium. The sample that has been mixed with the specific antisera in the segment is injected simultaneously by aspiration into 6 capillaries at the anodic end. The proteins are separated by electrophoresis at high voltage. The separated proteins

are detected at 200nm at the cathodic end of the capillary.

3. The reference pattern (ELP) is automatically overlayed with the antisera patterns (Ig G, Ig A, Ig M, Kappa and Lambda) allowing visualization of the disappearance or decrease of the suspected monoclonal component.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

i. Study design:

Within run reproducibility - Six serum samples were run 6 times within a run and the run was repeated with a different lot number antiserum. The six samples were comprised of one normal sample and five pathological samples (monoclonal IgG, IgA, IgM, kappa, lambda). According to the identified monoclonal protein, the concordant and reproducible within-run results were obtained.

Between run reproducibility - Nine serum samples were run 4 times and repeated in 3 runs on 3 different lot number antisera. The nine samples were comprised of 3 samples with a total Ig level of <0.8 g/dL: IgM K, Ig A L, and IgG K samples, 3 samples with total Ig level between 0.8 – 2 g/dL: IgG L, 2 IgA K, and IgM K samples, and 3 samples with total Ig level of >2.0 g/dL: IgA K, IgG L, and IgM L samples. According to the identified monoclonal component characterization, the concordant and reproducible between-run results were obtained.

b. Linearity/assay reportable range:

Not applicable.

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

No reference standards and method available.

d. Detection limit:

CAPILLARY IMMUNOTYPING detection limit results are listed below:

Sample No.	Monoclonal component			Detection limit (mg/dL)
	Type		Concentration (g/dL) (in the original serum)	
1	Ig A, K	Alpha	0.50	25
		Kappa		25
2	Ig G, L	Gamma	0.20	25
		Lambda		25
3	Ig M, K	Mu	0.39	25
		Kappa		25

The detection limit of a monoclonal component is about 25 mg/dL.

e. Analytical specificity:

The Immunotyping interference study test results cryoglobulins, hemolyzed and lipemic samples are as follows:

Interference	Number of samples	Results
Cryoglobulins	4	No effects
Hemoglobin	15	No effects
Lipids	7	No effects

* The system runs at 35.5° C which is warmer than room temperature 15°-30°. The voltage applied by the system to the sample is 7700volts. With the temperature control and applied voltage to the capillaries the system actually facilitates the migration of those samples that contain cryoglobulins, hemoglobin, or lipids. CAPILLARYS IMMUNOTYPING is based on the antigen-antibody complex migration pattern. Results are determined by the reduction and removal of the specific immunoglobulin which are not affected by cryoglobulins, hemoglobin or lipids.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

i. Study design: A total of 135 serum samples were performed on CAPILLARYS IMMUNOTYPING and HYDRAGEL 9 IF kits. 119 were pathological serum samples and 16 were normal serum samples. The CAPILLARYS IMMUNOTYPING method used the CAPILLARYS ß1-ß2^{+} buffer kit in this comparative study. There was 95% agreement between the two methods (see results below).

CAPILLARYS IMMUNOTYPING Samples – Interpretation Classification Summary

Qualitative Results	**Total**	**Complete Agreement**	**Partial Agreement**
Normal	16	16	0
IgG K	40	40	0
IgG L	20	20	0
IgA K	4	4	0
IgA L	8	8	0
IgM K	21	18	3*
IgM L	4	4	0
Free Kappa	1	1	0
Free Lambda	2	2	0
IgG (γ Heavy Chain)	1	1	0
IgG K/IgG L (Biclonal)	2	2	0
IgG K/IgM K (Biclonal)	2	2	0
IgG / IgG K	1	1	0
2 IgG L (Biclonal)	1	1	0
2 IgA K (Biclonal)	4	3	1*
IgA K/Ig M K (Biclonal)	1	1	0
3 IgA K (Triclonal)	2	2	0
IgM K / IgM L (Biclonal)	1	1	0
2 IgG K, 1 IgG L, 1 IgM K (Oligoclonal)	1	1	0
2 IgG K, 1 IgG L (Oligoclonal)	1		1**
3 IgG K, 2 IgG L (Oligoclonal)	1		1**

Qualitative Results	Total	Complete Agreement	Partial Agreement
IgG K, IgG L, 2 IgM K, IgM L (Oligoclonal)	1		1**
Grand Total	135	128	7*

Note: The 7 samples (4* with very small quantities of monoclonal on a high polyclonal and 3 ** oligoclonal profiles) demonstrated partial agreement. These samples exhibit profiles that were less discernable, due to low concentration (near or below the assay detection limit) of the monoclonal component. In all 128 cases, both techniques detected and characterized the monoclonal proteins (immunotyping) in human serum with complete agreement. (Characterization of some of these low concentration monoclonal proteins was very difficult to analyze, in spite of the software zoom feature application).

b. Matrix comparison:
Not applicable.

3. Clinical studies:
   a. Clinical Sensitivity:
   Not given.
   b. Clinical specificity:
   Not given.
   c. Other clinical supportive data (when a. and b. are not applicable):
   Not Applicable.
4. Clinical cut-off:
   Same as Expected values/Reference range.
5. Expected values/Reference range:
   Absence of monoclonal immunoglobulins.

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.