510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k130500

B. Purpose for Submission:

Modification of cleared devices and instruments: addition of CAPILLARYS 2 and CAPILLARYS 2 FLEX-PIERCING instruments to the cleared CAPILLARYS IMMUNOTYPING and IT/IF Control devices (k042939, k082085, k101863).

The three cleared instruments are CAPILLARYS (k042939, k082085) for Monoclonal Immunoglobulin (IgG, IgA, IgM, Kappa and Lambda) Immunotyping; CAPILLARYS 2 (k112491) and CAPILLARYS 2 FLEX-PIERCING (k112550 and k122101) for Hemoglobin electrophoresis (Hb normal, Hb variants and HbA1c).

C. Measurand:

Monoclonal Immunoglobulins (IgG, IgA, IgM, Kappa, Lambda) in serum and urine

D. Type of Test:

Capillary Zone Electrophoresis

E. Applicant:

SEBIA, INC.

F. Proprietary and Established Names:

CAPILLARYS IMMUNOTYPING (PN2100) and IT/IF Control (PN 4788) using the CAPILLARYS 2 Instrument (PN 1222) and CAPILLARYS 2 FLEX-PIERCING Instrument (PN 1227)

G. Regulatory Information:

1. Regulation section:

   21 CFR§ 866.5510 Immunoglobulins (A, G, M, D, E) Immunological Test Systems
   21 CFR§ 866.5550 Immunoglobulin (light chain specific) Immunological Test
   21 CFR§ 862.1630 Electrophoretic, Protein Fractionation
   21 CFR § 862.1660 Quality Control Material (assayed and unassayed)

2. Classification:

   Class II (test systems)
   Class I (control and Electrophoretic, protein fractionation devices)

3. Product code:

   CFF - Immunoelectrophoretic, Immunoglobulins (G, A, M)
   DFH – Kappa, Antigen, Antiserum, Control
   DEH – Lambda, Antigen, Antiserum, Control

CEF – Electrophoretic, Protein Fractionation
JJY – Multi-analyte controls, all kinds (assayed)

4. Panel:

   Immunology (82)
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   CAPILLARYS IMMUNOTYPING:

   The CAPILLARYS IMMUNOTYPING kit is designed for the detection and characterization of monoclonal proteins (immunotyping) in human urine and serum with the CAPILLARYS, the CAPILLARYS 2 and the CAPILLARYS 2 FLEX-PIERCING, SEBIA, for capillary electrophoresis. It is used in conjunction with the SEBIA CAPILLARYS PROTEIN(E) 6 kit, designed for protein separation into 6 major fractions in alkaline buffer (pH 10.0).

   The CAPILLARYS, CAPILLARYS 2 and the CAPILLARYS 2 FLEX-PIERCING perform all procedural sequences automatically to obtain a protein profile for qualitative analysis. Each urine or serum 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 proteins, 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.

   IT / IF CONTROL:

   The IT / IF Control is designed to quality control the qualitative detection and characterization of human monoclonal immunoglobulins (Ig G, Ig A, Ig M, Kappa and Lambda) with the electrophoresis methods:

   - Immunotyping performed using capillary electrophoresis on SEBIA CAPILLARYS 2 and CAPILLARYS 2 FLEX PIERCING instruments and on SEBIA MINICAP instrument,
   - Immunofixation methods: SEBIA HYDRAGEL IF, HYDRAGEL IF Penta, HYDRAGEL BENCE JONES (Standard mask and Dynamic mask) performed using the HYDRASYS and HYDRASYS 2 instruments and the K20 electrophoresis chamber.

   The IT / IF Control is designed for laboratory use. It should be used (with its barcode label for MINICAP procedure) like a human serum sample. The electrophoretic pattern obtained is specific for each batch of IT/IF control.
   For *In Vitro* Diagnostic Use.

2. Indication(s) for use:

   Same as Intended Use.

3. Special conditions for use statement(s):

   The device is for prescription use only.

4. Special instrument requirements:

   CAPILLARYS IMMUNOTYPING KIT:
   CAPILLARYS, CAPILLARYS 2 and CAPILLARYS 2 FLEX-PIERCING

   FOR IT/IF CONTROL:
   This device has been validated for use with the following SEBIA instruments:
   - CAPILLARYS 2 and CAPILLARYS 2 FLEX-PIERCING
   - MINICAP System (capillary electrophoresis) cleared in k073002
   - HYDRASYS 1 and HYDRASYS 2 (IF) cleared in k960029
   - K20 electrophoresis chamber (IF) cleared in k951536

I. Device Description:

The Capillarys Immunotyping (PN 2100) kit is designed for optimal performance on the SEBIA CAPILLARYS System (PN 1220) (k042839), an automated capillary electrophoresis system; CAPILLARYS 2 (PN 1222) (k112491) and CAPILLARYS 2 FLEX-PIERCING (PN 1227) (k112550 and k122101).

The Capillarys Immunotyping (PN 2100) kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human serum and urine (k042939 and k082939). 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 (free and bound) light chains, and lambda (free and bound) light chains.

The IT/IF Control is obtained from a pool of human sera complemented with monoclonal immunoglobulins displaying the 5 specificities G, A, M, Kappa and Lambda.

The IT/IF Control is supplied in a stabilized lyophilized form.

J. Substantial Equivalence Information:

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

   SEBIA Hydragel Immunofixation Kit, k960669
   SEBIA IT/IF Control, k101863

2. Comparison with predicate:

   CAPILLARYS IMMUNOTYPING:

Similarities		
Item	Device	Predicate
IFE Antisera Specificity	IgG, IgA, IgM heavy chains Kappa, Lambda light chains	Same
Sample type	Serum and Urine	Serum and urine
IFE Antisera Storage	2 – 8ºC or Room Temperature (15 – 30ºC)	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, CAPILLARYS 2 and CAPILLARYS 2 FLEX-PIERCING for capillary electrophoresis.	The HYDRAGEL 4 IF kit is 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	Serum and Urine Capillary Electrophoresis: Capillary Electrophoretic Migration with Immunofixation by Subtraction (Immunotyping).	SIFE and UIFE: Agarose gel Electrophoretic Migration with Immunofixation.
Methodology	Capillary Electrophoresis	Gel Electrophoresis
Equipment	Automated CAPILLARYS electrophoresis System	Semi-automated HYDRASYS electrophoresis apparatus
Sample size	240 µL	100 µL
Buffer pH	pH 10.0	pH 9.1
Interferences	Hemoglobin, Lipids, Bilirubin and Rheumatoid Factor	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

CAPILLARYS IT/IF CONTROL:

Similarities		
Item	Device	Predicate
Intended Use	For the detection and characterization of monoclonal immunoglobulins.	Same
Results	Qualitative Monoclonal Protein Interpretation	Same

Differences		
Item	Device	Predicate
Indication for Use/ Intended Use	The IT/IF Control is designed to quality control the qualitative detection and characterization of human monoclonal immunoglobulins (IgG, IgA, IgM, Kappa and Lambda) with the electrophoresis methods: - immunotyping performed using capillary electrophoresis on SEBIA CAPILLARYS 2 and CAPILLARYS 2 FLEX PIERCING instruments, SEBIA Minicap instrument. - immunofixation methods: SEBIA HYDRAGEL IF, HYDRAGEL IF Penta, HYDRAGEL BENCE JONES (Standard mask and Dynamic mask) performed using the HYDRASYS and HYDRASYS 2 instruments and the K20 electrophoresis chamber.	Paragon CZE® 2000 IFE/s (Immunofixation Electrophoresis by subtraction) Control is for use with the Paragon CZE® 2000 system and related IFE/s reagents to assure correct immunosubtraction by the system. The Control provides a qualitative test to identify human IgG kappa, IgA lambda, IgM kappa proteins by immunosubtraction.
Instrument(s)	Minicap Immunotyping (MiniCapillarys) instrument; Hydrasys and Hydrasys 2 electrophoresis instruments and the K20 electrophoresis chamber.	Paragon CZE® 2000 IFE/s
Matrix	Human serum	Human plasma
Form	Lyophilized	Liquid
Packaging and Volume	1 bottle reconstituted to 1 mL	3 bottles x 3 mL each
Storage Stability	Lyophilized at 2-8°C for 3 years. Reconstituted aliqouts at 2-8°C for 1 week; Reconstituted aliquots at -18 to -22°C for 2 months Frreze/ thaw cycle: 20 cycles	Unopened bottles at 2-8°C for 18 months. Opened bottles at 2-8°C for 45 days.
Preparation for Use	Use upon reconstitution	Use upon 1:2 dilution

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 (IgG), alpha (IgA), mu (IgM) 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 immunoglobulin concentrations.
   « HYPERGAMMA » if total immunoglobulins level is > 2 g/dL (hypergammaglobulinemia),
   « HYPOGAMMA » if total immunoglobulins level is < 0.8 g/dL (hypogammaglobulinemia),
   « STANDARD » if total immunoglobulin 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 (IgG, IgA, IgM, 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:

Within run reproducibility of immunotyping kit on CAPILLARYS 2 instrument: Three IT/IF control lots were run 6 times within a run and the run was repeated with three different immunotyping antisera lot numbers. The IT/IF controls were comprised of one monoclonal IgGL, IgAL, and IgMK. According to the identified monoclonal protein, the concordant and reproducible within-run results were obtained.

Between-run and between-lot reproducibility of immunotyping kit on CAPILLARYS 2 instrument: Three pathological serum samples and three pathological urine samples were run 3 times and repeated in 3 different runs on 3 different immunotyping antisera lot numbers. The three pathological serum samples were comprised of IgML, IgAK, and IgGK samples. The three pathological urine samples were comprised of one IgGL with one free Lambda, two free Kappa and one free Lambda. According to the identified monoclonal component characterization, concordant and reproducible between-run results were obtained for both pathological serum and urine samples.

Between run and between lot reproducibility of IT/IF Control on CAPILLARYS 2 instrument: Three lots of IT/IF Control were run 3 times and repeated in 3 different runs on 3 different immunotyping antisera lot numbers. Identification and characterization of specific monoclonal proteins were reproducibly obtained in the SEBIA IT/IF control using the CAPILLARYS 2 instrument.

b. Linearity/assay reportable range:

Not applicable.

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

No reference standards and methods available.

d. Detection limit:

CAPILLARY IMMUNOTYPING detection limit results using CAPILLARY 2 are listed below:

Sample No.	**Monoclonal component**			**Detection limit (mg/dL)**
	Type		**Concentration (g/dL) (in the original serum)**	
1	IgA, L	Alpha	0.24	50
		Lambda		50
2	IgG, K	Gamma	3.02	25
		Kappa		25
3	IgM, L	Mu	1.46	25
		Lambda		25

e. Analytical specificity:

The Immunotyping interference study test results with interferents using CAPILLARY 2 instrument: hemoglobin, lipids (cholesterol and triglycerides), bilirubin and rheumatoid factor in serum samples (representing the 6 monoclonal protein specificities: IgGK IgGL, IgAK, IgAL, IgMK and IgML) are as follows:

Immunotyping Interference Study

Interferents	Number samples	Results
Hemoglobin (4 g/L)	15	No effects
Lipids (Cholesterol: 8.24 mmol/L and triglycerides: 11.58 mmol/L)	8	No effects
Bilirubin (293 and 377 µmol/L)	8	No effects
Rheumatoid Factor (2178 IU/mL)	6	No effects

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

i. Serum samples

A total of 86 serum samples (60 pathological, 1 polyclonal and 25 normal) were performed on CAPILLARYS IMMUNOTYPING and HYDRAGEL 4 IF kits using CAPILLARYS 2 and HYDRASYS. There was 100% agreement between the two methods (see results below).

CAPILLARYS IMMUNOTYPING Serum Samples using CAPILLARYS 2 vs. HYDRASYS – Interpretation Classification Summary

Qualitative Results	**Total**	**Complete Agreement**
Normal	25	Complete Agreement
IgG Kappa	19	Complete Agreement
IgG Lambda	13	Complete Agreement
IgA Kappa	4	Complete Agreement
IgA Lambda	5	Complete Agreement
IgM Kappa	7	Complete Agreement
IgM Lambda	2	Complete Agreement
Free Kappa	1	Complete Agreement
Free Lambda	2	Complete Agreement
IgG Kappa / IgG Lambda	1	Complete Agreement
IgG Kappa / IgA Kappa	1	Complete Agreement
2 IgA Kappa (Biclonal)	3	Complete Agreement
Oligoclonal	1	Complete Agreement
2 IgM Kappa (Biclonal)	2	Complete Agreement

Qualitative Results	Total	Complete Agreement
Grand Total	86	Complete Agreement

ii. Urine samples

A total of 51 urine samples (26 pathological with 17 had 1 or more Kappa or Lambda monoclonal proteins and 25 normal) were performed on CAPILLARYS IMMUNOTYPING and HYDRAGEL 4 IF kits using CAPILLARYS 2 and HYDRASYS. There was 100% agreement between the two methods (see results below).

Qualitative Results	Total	Complete Agreement
Normal	25	Complete Agreement
IgG Kappa	3	Complete Agreement
IgA Lambda	1	Complete Agreement
Free Kappa	3	Complete Agreement
Free Lambda	3	Complete Agreement
Several Free Kappa	8	Complete Agreement
Several Free Lambda	3	Complete Agreement
IgG Lambda / Lambda Free	3	Complete Agreement
IgG Kappa / Kappa Free	2	Complete Agreement
Grand Total	51	Complete Agreement

iii. Method Comparison between CAPILLARYS 2 and CAPILLARYS 2 Flex-Piercing on serum samples

A total of 56 serum samples (46 pathological and 10 normal) were performed on CAPILLARYS IMMUNOTYPING using CAPILLARYS 2 and CAPILLARYS 2 Flex-Piercing. There was 100% agreement between the two methods (see results below).

Qualitative Results	Total	Complete Agreement
Normal	10	Complete Agreement
IgG Kappa	20	Complete Agreement
IgG Lambda	12	Complete Agreement
IgA Kappa	1	Complete Agreement
IgA Lambda	2	Complete Agreement
IgM Kappa	4	Complete Agreement
IgG Kappa / IgM Kappa	1	Complete Agreement
IgG Kappa / IgA Kappa	1	Complete Agreement
2 IgA Kappa (Biclonal)	1	Complete Agreement
IgM Kappa / IgM Lambda	1	Complete Agreement
Lambda	2	Complete Agreement
2 Lambda	1	Complete Agreement

Qualitative Results	Total	Complete Agreement
Grand Total	56	Complete Agreement

iv. Method Comparison between CAPILLARYS 2 and CAPILLARYS 2 Flex-Piercing on urine samples

A total of 55 urine samples (26 pathological with 17 had 1 or more Kappa or Lambda monoclonal proteins and 25 normal) were performed on CAPILLARYS IMMUNOTYPING using CAPILLARYS 2 and CAPILLARYS 2 Flex-Piercing.. There was 100% agreement between the two methods (see results below).

Qualitative Results	Total	Complete Agreement
Normal	3	Complete Agreement
IgG Kappa	3	Complete Agreement
IgG Lambda	1	Complete Agreement
IgG Kappa / 2 kappa free	1	Complete Agreement
IgG Kappa / kappa free	2	Complete Agreement
kappa free / 2 lambda free	1	Complete Agreement
IgG Lambda / 2 lambda free	2	Complete Agreement
IgG Lambda / lambda free	1	Complete Agreement
IgA Kappa / kappa free	1	Complete Agreement
Free Kappa	6	Complete Agreement
Free Lambda	7	Complete Agreement
Several Free Kappa	14	Complete Agreement
Several Free Lambda	6	Complete Agreement
Abnormal with no reaction	1	Complete Agreement
Polyclonal	6	Complete Agreement
Grand Total	55	Complete Agreement

v. Comparative study between SEBIA IT/IF Control and Beckman Paragon CZE 2000 IFE Control on CAPILLARYS 2 instrument

Three different lots of SEBIA IT/IF Control (IgGL, IgAL and IgMK) were compared to the Beckman CZE 2000 IFE Control (IgGK, IgAL, and IgMK). Complete identification and characterization of specific monoclonal proteins in both the SEBIA IT/IF control and Beckman Paragon CZE 2000 IFE Control were obtained as defined in the package inserts of both controls using the CAPILLARYS IMMUNOTYPING kit on the CAPILLARYS 2 instrument.

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. Instrument Name:

SEBIA CAPILLARYS 2 AND CAPILLARYS 2 FLEX-PIERCING

O. System Descriptions:

1. Modes of Operation:

   Closed tube batch mode with the following automated steps:

   - Bar code reading of sample tubes (up to 8 tubes) and sample racks
   - Sample injection from primary tubes into antisera segments
   - Direct detection of monoclonal proteins by Immunotyping

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X_____ or No _____

3. Specimen Identification:

   Bar code reader

4. Specimen Sampling and Handling:

   Closed or open tubes are placed in the sample racks

5. Calibration:

   Not applicable

6. Quality Control:

   IT/IF Control analysis

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

The CAPILLARYS IMMUNOTYPING using the CAPILLARYS 2 and the CAPILLARYS 2 FLEX-PIERCING instruments is a modification of previously cleared CAPILLARYS IMMUNOTYPING using the CAPILLARYS instrument (k042939, k082085) for the detection and characterization of monoclonal proteins in serum and urine. The SEBIA Hydragel Immunofixation Kit (k960669) was used as a comparative method for detection of the monoclonal proteins.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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