

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

A. 510(k) Number:

k082085

B. Purpose for Submission:

Device modification (addition of urine as sample matrix)

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
Systems

21 CFR§ 866.5550 Immunoglobulin (light chain specific) Immunological Test

21 CFR§ 862.1630 Electrophoretic, Protein Fractionation

2. Classification:

Class 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:

The CAPILLARYS IMMUNOTYPING kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human urine and serum with the CAPILLARYS System, SEBIA, for capillary electrophoresis. It is used in conjunction with the CAPILLARYS PROTEIN (E) 6 kit, SEBIA, designed for 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 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.

2. Indication(s) for use:
Same as Intended use.
3. Special conditions for use statement(s):
For prescription only.
4. Special instrument requirements:
SEBIA CAPILLARYS System

I. Device Description:

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

Other reagents required but not supplied: CAPILLARYS PROTEIN(E) 6 kit (SEBIA PN 2003), CAPILLARYS URINE kit (PN 2012) distilled or deionized water, CAPICLEAN (SEBIA PN 2058), Sodium Hypochlorite solution (for sample probe cleaning), CAPILLARYS wash solution (SEBIA PN 2052), CAPILLARYS Dialysis System (PN 9200).

J. Substantial Equivalence Information:

1. Predicate device name(s):
SEBIA HYDRAGEL 9 Bence Jones kit
Sebia Hydragel Immunofixation Kit
2. Predicate K number(s):
k972591 (BJ)
k960669 (IFx)
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Electrophoretic separation/fractionation of urine proteins	Qualitative visual detection of protein abnormalities	Same
IFE Antisera Specificity	Antibody specificity to heavy chains (IgG, IgA, IgM) and to light chains (Kappa, Lambda).	Same
IFE Antisera Storage	2 – 8°C or Room Temperature (15 – 30°C)	Same
Sample matrices	Serum and Urine	Same
Results	Qualitative Interpretation	Same

Differences		
Item	Device	Predicate
Intended Use	The CAPILLARYS IMMUNOTYPING kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human urine or serum with the SEBIA CAPILLARYS System, for capillary electrophoresis.	The HYDRAGEL Bence Jones Dynamic Mask kit is designed for qualitative detection and identification of Bence Jones proteins, monoclonal free light chains kappa or lambda in human urine or serum; and the HYDRAGEL 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	SIFE/s: Capillary Electrophoretic Migration with Immunofixation by Subtraction (Immunotyping).	Agarose gel electrophoretic migration with immunofixation
Methodology	Capillary electrophoresis	Gel electrophoresis
Equipment	CAPILLARYS, SEBIA	HYDRASYS, SEBIA
Analyzed sample	1 sample per antisera segment	1, 2, 4, or 9 samples according to the gel configurations
Lowest detection limit	2.5 mg/dL	3.0-12.0 mg/dL

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

None provided.

L. Test Principle:

Protein electrophoresis is a well established technique routinely used in clinical laboratories for screening serum samples for protein abnormalities. The CAPILLARYS System, SEBIA, for capillary electrophoresis has been developed to provide complete automation of this testing with fast separation and good resolution. In many aspects, the methodology can be considered as an intermediary between classical zone electrophoresis and liquid chromatography.

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.

In capillary electrophoresis, abnormal fractions in serum protein electrophoregrams, primarily those in the beta globulin and gamma globulin zones, are always suspected of being monoclonal proteins (M-proteins, paraproteins, monoclonal immunoglobulins) and therefore, an indication of monoclonal gammopathies. With CAPILLARYS IMMUNOTYPING and CAPILLARYS IMMUNOTYPING URINE procedures, the immunotyping is performed with specific antibodies to identify these abnormal fractions.

The CAPILLARYS system has 6 capillaries functioning in parallel. In this system, a sample dilution is prepared and injected simultaneously by aspiration at the anodic end of the 6 capillaries, 3 times successively. For the immunotyping, the reference pattern (ELP pattern) is obtained by injection of the sample mixed with ELP solution in a capillary No. 1 providing a complete electrophoretic pattern of sample 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.

The superimposition of the antisera patterns with the ELP pattern allows for visualization of the disappearance and / or the decrease of a monoclonal fraction on the antiserum pattern and to indicate a gammopathy.

NOTE : In CAPILLARYS IMMUNOTYPING procedure, 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 serum sample immunoglobulins and the specific antiserum) has a very anodic mobility (between alpha-1 zone and albumin or more anodic than albumin).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Study design:

Within run precision: six different pathological urine samples containing one or two monoclonal components and one normal urine sample were run 6 times within a run and the runs were repeated with two different lot number antiserum. The six samples were comprised of one normal sample and five pathological samples (monoclonal IgG κ ; IgA λ with one free λ light chain; IgM κ ; Kappa with two κ light chains; and Lambda with one λ light chain).

According to the identified monoclonal protein, the concordant and reproducible within-run results were obtained.

Between run reproducibility – Eight urine samples were run 4 times and repeated in 4 runs on 3 different lot number antisera. The seven urine samples were comprised of normal, one IgG λ , three Kappa and three Lambda free light chains. According to the identified monoclonal component characterization, the concordant and reproducible between-run results were obtained.

Validation on Hydrigel Dynamic mask:

Validation data were requested and submitted on the Hydrigel Dynamic mask (2003 validation data on slight modification to the Hydrigel Standard mask).

The slight modification is using a colored reference guide for reagent application, an antisera segment, a segment holder, a dynamic mask guide and a length reducing device. The reagents are applied using the wells of the antisera segment which is moved over the gel surface compared to the standard mask wherein the reagents are applied using troughs of the template. Concordance study had a total of 20 serum samples and 36 urine samples (31 pathological, and 5 normal) were performed on HYDRAGEL Bence Jones standard mask and dynamic mask using the HYDRAGEL System. The study demonstrated 100% agreement between the two methods.

b. Linearity/assay reportable range:

Not applicable.

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

Not applicable

d. Detection limit:

The detection limit was determined by testing serial two-fold dilutions prepared from two pathological urine sample containing Kappa and Lambda free light chain (at concentration about 55 mg/dL and 24 mg/dL respectively). It was diluted with saline and analyzed using the CAPILLARYS Immunotyping procedure. The minimal detection limit of the monoclonal component was about 2.5 mg/dL.

e. Analytical specificity:

There was no need to test drugs and salts interferences because these are eliminated during dialysis. However, hemoglobin is commonly known to co-migrate with transferrin if not removed by dialysis. Hemoglobin interference study was not evaluated for this assay. The Limitation section of the package insert states: “Hemoglobin is commonly known to co-migrate with transferrin when it is in the urine sample. It is advised to observe the urine sample features after the first centrifugation (5000 rpm for 10 minutes) (e.g., signs of red blood cells and/or hemolysis in the urine sample)”.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Study design: A total of 61 urine samples (33 pathological, 22 polyclonal and 6 normal) were performed on CAPILLARYS IMMUNOTYPING kits using the CAPILLARYS System and on HYDRAGEL Bence Jones and HYDRAGEL IF kits using the HYDRAGEL System. The total protein concentrations ranged from 10.0 – 2340 mg/dL. The study demonstrated 100% agreement between the two methods (see results below).

Qualitative Results	Total	Complete Agreement
Normal	6	6
Polyclonal IgG κ + IgG λ	15	15
Polyclonal IgG κ	3	3
Polyclonal IgG, IgA, IgM, Kappa and Lambda	1	1
Polyclonal Kappa	1	1
Polyclonal IgG	2	2
Monoclonal Lambda free light chains	10	10
Monoclonal Kappa free light chains	6	6
Monoclonal IgG λ + Lambda free light chains	8	8
Monoclonal IgA λ + Lambda free light chains	1	1
Monoclonal IgA κ + Kappa free light chains	1	1
Monoclonal IgM κ + Kappa free light chains	1	1
Monoclonal IgG κ	2	2
Monoclonal IgG λ	3	3
Monoclonal IgA κ	1	1
Grand Total	61	61

- 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 urine Bence Jones proteins.

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.