

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

A. 510(k) Number:

k082388

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:

MINICAP IMMUNOTYPING (PN 2300)

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 code:

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 MINICAP IMMUNOTYPING kit is designed for the detection and the characterization of monoclonal proteins (immunotyping) in human serum with the MINICAP System, SEBIA, for capillary electrophoresis. It is used in conjunction with the MINICAP PROTEIN (E) 6 kit, SEBIA, designed for serum proteins separation into 6 major fractions in alkaline buffer (pH 9.9).

The MINICAP system performs all procedural sequences automatically to obtain a protein profile for qualitative analysis. Each 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 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 suspected monoclonal proteins.

For *in vitro* diagnostic use only.

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:
This device has been validated for use with the SEBIA MINICAP System (capillary electrophoresis) which was cleared in k082227.

I. Device Description:

The MINICAP IMMUNOTYPING kit (PN 2300) kit contains seven ready to use components: sample diluent supplied in 6 vials, 4 mL each; ELP Solution supplied in 1 vial, 1.2 mL; and 5 antisera tubes with specific antibodies against gamma (IgG), alpha (IgA) mu (IgM) heavy chains and kappa (free and bound) light chains, and lambda (free and bound) light chains, supplied in 1 tube, 1.2 mL each.

J. Substantial Equivalence Information:

1. Predicate device name(s):
CAPILLARYS IMMUNOTYPING, PN 2100
2. Predicate 510(k) number(s):
k042939
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For the detection and the characterization of monoclonal proteins (immunotyping) in human serum	Same
Methodology	Capillary electrophoresis	Same
Technology	SIFE/s: Capillary Electrophoretic Migration with Immunofixation by Subtraction (Immunotyping).	Same
Absorbance wave length	200 nm	Same
Sample type	Serum	Same
Introduction of the sample into the automatic system	Continuous loading	Same
Sample identification	Yes	Same
Antisera Specificity	Antibody specificity to heavy chains (IgG, IgA, IgM) and to light chains (Kappa, Lambda).	Same
Antisera Storage	2 – 8°C	Same
Buffer pH	pH 9.9	Same

Similarities		
Item	Device	Predicate
Lowest detectible Limit	25 mg/dL	Same
Results	Qualitative Interpretation	Same

Differences		
Item	Device	Predicate
Instrument	MINICAP System	CAPILLARYS System
Number of separation units	2 parallel capillaries	6 parallel capillaries
Number of analysis (throughput)	2 samples/hour	8 samples/hour
Immunotyping antisera	Antisera tubes	Antisera segments
Buffer reagent	2 vials of 250 mL	2 vials of 700 mL
Wash solution	1 vial of 25 mL Stock solution	1 vial of 75 mL Stock solution
Serum sample volume required for dilution: dependent on immunoglobulin concentration)	<0.8 g/dL Ig: 30 µL of serum required to make 1:10 dilution 0.8-2.0g/dL Ig: 15 µL of serum to make 1:20 dilution; and >2.0g/dL Ig: 10 µL of serum to make 1:40 dilution	<0.8 g/dL Ig: 40 µL of serum required to make 1:10 dilution 0.8-2.0g/dL Ig: 20 µL of serum to make 1:20 dilution; and >2.0g/dL Ig: 20 µL of serum to make 1:40 dilution

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

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices - Guidance for Industry and FDA Staff, May 11, 2005.

L. Test Principle:

Protein electrophoresis is a well established technique routinely used in clinical laboratories for screening serum samples for protein abnormalities. The MINICAP 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 MINICAP 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 MINICAP IMMUNOTYPING procedure, the immunotyping is performed with specific antibodies to identify these abnormal fractions.

The MINICAP system has 2 capillaries functioning in parallel. In this system, a sample dilution is prepared and injected simultaneously by aspiration at the anodic end of the 2 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 providing a complete electrophoretic pattern of sample proteins. The antisera patterns are obtained with the 5 following analyses, by injection in capillaries 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 MINICAP 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 reproducibility - Four serum samples were run 6 times within a run and the run was repeated with a different lot number antiserum. The four samples were comprised of one normal sample and three pathological samples: monoclonal IgG Lambda, IgA Kappa, and IgM Kappa. According to the identified monoclonal protein, the concordant and reproducible within-run results were obtained.

Between run reproducibility - Three serum samples were run 4 times and repeated in 3 runs on 3 different lot number antisera. The three samples were comprised of one IgG Kappa, one IgM Kappa and one IgA Lambda (with two monoclonal components) and had a total Ig levels between 0.8 g/dL to 2 g/dL. 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:*
MINICAP 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, L	Alpha	2.7
		Lambda	
2	Ig G, K	Gamma	25
		Kappa	25
3	Ig M, K	Mu	25
		Kappa	25

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

- e. *Analytical specificity:*
Interference by endogenous substances: Seven samples comprised of one normal and six pathological sera (IgG κ , IgG λ , IgA κ , IgA λ , IgM κ , IgM λ) were spiked with endogenous substances namely hemoglobin, total cholesterol and total triglyceride and tested on MINICAP Immunotyping device. No effects were observed with hemoglobin (up to 4 g/L), total cholesterol (up to 3.17 g/L) and total triglyceride (up to 10.16 g/L). The package insert states to avoid aged improperly stored serum samples, beta fractions would be modified and to avoid plasma samples, fibrinogen migrates in beta-2 position (shoulder on beta-2); interferences due to bilirubin have not been studied for the MINICAP IMMUNOTYPING PROCEDURE; it is advised to observe the serum sample features; when an interferent fraction is suspected, it is recommended to perform again the analysis on the serum sample or to use complementary studies with other techniques.
- f. *Assay cut-off:*
Not applicable
2. Comparison studies:
- a. *Method comparison with predicate device:*
Study design: A total of 69 serum samples (57 pathological and 12 normal) were performed on MINICAP IMMUNOTYPING using the MINICAP System and on the CAPILLARYS IMMUNOTYPING kits using the CAPILLARYS System. The study demonstrated 100% agreement between the two methods (see results below).

Qualitative Results	Total	Complete Agreement
Normal	12	12
IgG κ	23	23
IgG κ + 2 κ (not GAM)	1	1
IgG λ	15	15
IgA κ	5	5
IgA κ (Biclonal)	3	3
IgA λ (Biclonal)	2	2
IgM κ	6	6
IgM λ	1	1
IgM λ + 2 IgM λ	1	1
Grand Total	69	69

- 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:

MINICAP System, SEBIA PN 1230

O. System Descriptions:

- 1. Modes of Operation:
Batch mode with the following sequence of automated steps:
Bar code reading of serum sample tubes (up to 18), reagent tubes and rotating sampler
Sample dilution from primary tubes in reagent cups
Capillary washing
Injection of diluted samples
Protein separation and direct detection of the separated proteins on capillaries
- 2. Software:
The SEBIA MINICAP operating system software is designed to work with the instrumentation, MINICAP. The MINICAP instrumentation directed by the PHORESIS software is fully automated in the performance of the sample identification by barcode labelling, dilution, testing, and calculation of results. The PHORESIS software utilizes Windows 98 or XP as the operating system with

Intel based processors with Visual Basic as the programming language.
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

3. Specimen Sampling and Handling:

Fresh serum samples are recommended for analysis. Samples may be stored for up to 10 days between 2 and 8°C. For longer storage, samples should be frozen within 8 hours of collection. Frozen sera are stable for one month.

Undiluted serum samples from primary tubes are automatically diluted according to the Immunoglobulin (Ig) concentration: 1:10 dilution on <0.8 g/dL Ig using 30 µL of serum to make dilution; 1:20 dilution on 0.8-2.0g/dL using 15 µL of serum; and 1:40 dilution on >2.0g/dL using 10 µL of serum.

5. Calibration:

Not applicable.

6. Quality Control:

It is necessary to use the ELP solution as the reference electrophoretic pattern of the sample proteins. Superimposition of the antisera patterns with the ELP pattern allows for visualization of the disappearance and/ or the decrease of a monoclonal fraction of the antiserum pattern and to indicate a gammopathy.

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

None.

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.