

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
 DECISION SUMMARY
 ASSAY ONLY**

I Background Information:

A 510(k) Number

K192095

B Applicant

Sebia

C Proprietary and Established Names

CAPi 3 Immunotyping, CapillaryS 3 Tera

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CFF	Class II	21 CFR 866.5510 - Immunoglobulins A, G, M, D, And E Immunological Test System	IM - Immunology
DFH	Class II	21 CFR 866.5550 - Immunoglobulin (light chain specific) immunological test system	IM - Immunology
DEH	Class II	21 CFR 866.5550 - Immunoglobulin (light chain specific) immunological test system	IM - Immunology
CEF	Class I	21 CFR 862.1630 - Protein (fractionation) test system	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Addition of a new matrix (urine) to a previously cleared device.

B Measurand:

Monoclonal Immunoglobulins (IgG, IgA, IgM, Kappa, Lambda)

C Type of Test:

Capillary Zone Electrophoresis

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The CAPI 3 IMMUNOTYPING kit is designed for the qualitative detection and the characterization of monoclonal proteins (immunotyping) in human urine and serum with the CAPILLARYS 3 TERA instrument, SEBIA, for capillary electrophoresis. It is used in conjunction with the CAPI 3 PROTEIN(E) 6 kit, SEBIA, designed for proteins separation into 6 major fractions in alkaline buffer (pH 9.9). The CAPILLARYS 3 TERA instrument 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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

CAPILLARYS 3 TERA instrument

IV Device/System Characteristics:

A Device Description:

The CAPI 3 IMMUNOTYPING kit includes the following components:

- Sample diluent
- Pierceable cap for the Sample diluent vial
- Rack with electrophoresis (ELP) solution and antiserum tubes
- ELP solution
- Mammalian immunoglobulins antihuman gamma heavy chains
- Mammalian immunoglobulins antihuman alpha heavy chains
- Mammalian immunoglobulins antihuman mu heavy chains
- Mammalian immunoglobulins antihuman kappa (free and bound) light chains
- Mammalian immunoglobulins antihuman lambda (free and bound) light chains

B Principle of Operation:

The CAPILLARYS 3 TERA instrument uses the principle of capillary electrophoresis in a liquid medium. With this technique, charged molecules are separated by their electrophoretic mobility in an alkaline buffer with a specific pH. Protein separation is performed in a high voltage electrical field. The separated proteins are directly detected using absorbance at 200 nm at the cathodic end of the capillary. Separation occurs according to the electrolyte pH and is driven by electroosmotic flow. The CAPILLARYS 3 TERA instrument has silica capillaries functioning in parallel allowing 12 simultaneous analyses.

With the CAPI 3 IMMUNOTYPING procedure, the immunotyping using specific antibodies is performed to identify abnormal fractions in serum or urine protein profiles through a process called Immunofixation by Subtraction (Immunotyping). Here, the addition of immunoglobulin class specific antisera to the patient sample causes a shift in the electrophoretic mobility of the specific peaks, allowing the identification of the class of the aberrant peak.

C Instrument Description Information:

Modes of Operation	Yes	No
Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Software		
FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types.	<input checked="" type="checkbox"/>	<input type="checkbox"/>

V Substantial Equivalence Information:

A Predicate Device Name(s):

Capillarys Immunotyping, Capillarys 2 Instrument, IT/IF Control, Capillarys 2 Flex Piercing Instrument

CAPI 3 Immunotyping, Capillarys 3 Tera, IT/IF Control

B Predicate 510(k) Number(s):

K130500

K161928

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K192095</u>	<u>K130500</u>	<u>K161928</u>
Device Trade Name	IMMUNOTYPING, CAPILLARYS 3 TERA, IT/IF Control	CAPILLARYS IMMUNOTYPING and IT/IF Control using the CAPILLARYS 2 Instrument and CAPILLARYS 2 FLEX-PIERCING Instrument	CAPI 3 IMMUNOTYPING, CAPILLARYS 3 TERA, IT/IF Control
General Device Characteristic Similarities			
Intended Use/Indications For Use	<p>The CAPI 3 IMMUNOTYPING kit is designed for the qualitative detection and the characterization of monoclonal proteins (immunotyping) in human urine and serum with the CAPILLARYS 3 TERA instrument, SEBIA, for capillary electrophoresis. It is used in conjunction with the CAPI 3 PROTEIN(E) 6 kit, SEBIA, designed for proteins separation into 6 major fractions in alkaline buffer (pH 9.9).</p> <p>The CAPILLARYS 3 TERA instrument performs all procedural sequences automatically</p>	<p>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).</p> <p>The CAPILLARYS,</p>	<p>The CAPI 3 IMMUNOTYPING kit is designed for the qualitative detection and characterization of monoclonal proteins (immunotyping) in human serum with the CAPILLARYS 3 TERA instrument, SEBIA, for capillary electrophoresis. It is used in conjunction with CAPI 3 PROTEIN(E) 6 kit, SEBIA, designed for protein separation into 6 major fractions in alkaline buffer (pH 9.9).</p> <p>The CAPILLARYS 3 TERA instrument performs all procedural sequences automatically to obtain a protein</p>

	<p>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.</p> <p>The proteins, separated in silica capillaries, are directly detected by their absorbance at 200 nm.</p> <p>The electropherograms are evaluated visually to detect the presence of specific reactions with the suspect monoclonal proteins.</p> <p>For In Vitro Diagnostic Use.</p>	<p>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 electropherograms are evaluated visually to detect the presence of specific reactions with the suspect monoclonal proteins.</p> <p>For In Vitro Diagnostic Use.</p>	<p>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 (free and bound) light chains and lambda (free and bound) light chains, respectively.</p> <p>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.</p> <p>For In Vitro Diagnostic Use.</p>
Quality Control	The IT/IF Control	<p>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:</p> <p>-</p> <p>Immunotyping performed using capillary electrophoresis on SEBIA CAPILLARYS 2 and CAPILLARYS 2 FLEX</p>	<p>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:</p> <p>- Immunotyping performed using capillary electrophoresis on SEBIA CAPILLARYS 2, CAPILLARYS 2 FLEX-PIERCING and CAPILLARYS 3 TERA instruments and on SEBIA MINICAP</p>

		<p>PIERCING instruments and on SEBIA MINICAP instrument,</p> <p>- 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.</p> <p>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.</p> <p>For In Vitro Diagnostic Use.</p>	<p>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.</p> <p>The IT/IF Control is designed for laboratory use. It should be used (with its barcode label for CAPILLARYS and MINICAP procedure) like a human serum sample. The electrophoretic pattern obtained is specific for each batch of IT/IF control.</p> <p>For <i>In Vitro</i> Diagnostic Use.</p>
Separation system	<p>Free solution capillary electrophoresis (FSCE): protein separation in an alkaline buffer (pH 9.9) according to their charge, to the electrolyte pH and electroosmotic flow. Provides fast separation and good resolution. Electrophoregrams show separated fractions according to their charge.</p>	Same	Same
Sample Type	Serum and Urine	Same	Serum
Results	Qualitative	Same	Same
Reagent	Mammalian	Same	Same

	immunoglobulins anti-human gamma heavy chains, mammalian immunoglobulins antihuman alpha heavy chains, mammalian immunoglobulins antihuman mu heavy chains, mammalian immunoglobulins anti-human kappa (free and bound) light chains, mammalian immunoglobulins antihuman lambda (free and bound) light chains		
Sample Type	Serum and Urine	Same	Serum
Results	Qualitative	Same	Same
Reagent	Mammalian immunoglobulins anti-human gamma heavy chains, mammalian immunoglobulins antihuman alpha heavy chains, mammalian immunoglobulins antihuman mu heavy chains, mammalian immunoglobulins anti-human kappa (free and bound) light chains, mammalian immunoglobulins antihuman lambda (free and bound) light chains	Same	Same
Temperature Control	Peltier device	Same	Same
Software for data processing	SEBIA PHORESIS software	Same	Same
General Device Characteristic Differences			
Reagent format	CAPILLARYS 3 Immunotyping Kit: Sample diluent Rack with ELP solution tube and antiserum tube	CAPILLARYS IMMUNOTYPING Kit: Antisera segment containing ELP solution	One vial (lyophilized; 1.0 mL)
Instrument	SEBIA CAPILLARYS	SEBIA CAPILLARYS 2	Same

	3 TERA	FLEX-PIERCING SEBIA CAPILLARYS 2	
Analysis throughput	21 analyses / 2 hours	16 analyses / 2 hours	Same
Interface	PC interface + touch screen	PC interface	Same
Detection system	Deuterium lamp and LED	Deuterium lamp	Same
Firmware	Included into the instrument	Included into the PHORESIS software	Same
Number of separation units	12 parallel capillaries	8 parallel capillaries	Same
Sample tubes	uncapped tubes or capped tubes depending on the procedure	Same	Same
Sample identification	Bar code reading on sample tubes and RFID labels on sample racks	Bar code reading on both sample racks and tubes	Same
Reagent identification	Yes (RFID labels on reagent vials)	No	Same
Introduction of the samples into the automatic system	Primary maximal capacity of 120 tubes (i.e. 15 sample racks), uninterrupted throughput on sample racks (8 positions available).	Primary capacity of 13 tubes for IT technique (i.e. 13 sample racks), uninterrupted throughput on sample racks. Only position 1 on the sample rack contains sample tube.	Same
Reagent bay: main compartment	Up to four analysis buffers or hemolysing solutions (identified by RFID labels); one waste container, one container for the wash solution	CAPILLARYS 2 : Contains one vial of water, wash solution and buffer container. CAPILLARYS 2 FLEX-PIERCING : Contains one vial of water, wash solution, hemolyzing solution (for Hb and Hb A1c techniques) and buffer container.	Same
Reagent bay: secondary compartment	Up to 3 vials and 1 rack with immunotyping reagents (all RFID tagged) in temperature-controlled environment (< 15 °C); one RFID labeled vial and three tubes (for maintenance	N/A	Same

	solutions) at room temperature		
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VI Standards/Guidance Documents Referenced:

Not applicable

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

All results met the manufacturer’s pre-specified acceptance criteria.

Repeatability

Four different urine samples with monoclonal proteins including Bence Jones proteins were run using the CAPI 3 IMMUNOTYPING URINE procedure on all capillaries of the same CAPILLARYS 3 TERA instrument using one lot of CAPI 3 IMMUNOTYPING kit. The four samples included IgG-kappa, Lambda Free, IgM-kappa + kappa free, and IgA-Lambda + lambda free. Each sample was analyzed with each reagent in duplicate (ELP solution, Anti-Ig G, Anti-Ig A, Anti-Ig M, Anti-Kappa and Anti-Lambda using the 12 capillaries. In this study all dilution programs were tested. For each tested reagent, all samples gave concordant results within run and between capillaries.

Between-Instrument and Between-Lot Precision

Three different urine samples with monoclonal proteins including Bence Jones proteins were run using the CAPI 3 IMMUNOTYPING URINE procedure on three CAPILLARYS 3 TERA instruments and with three lots of CAPI 3 IMMUNOTYPING kit. The samples included one sample with two kappa free light chains, one sample with IgG-kappa immunoglobulin and one sample with Lambda free light chain. Each sample was analyzed on 18 runs over five working days (2 runs/day x 3 lots x 3 instruments = 18). In this study, all dilution programs were tested. All samples gave concordant results for all runs on the three CAPILLARYS 3 TERA instruments and with the three lots of CAPI 3 IMMUNOTYPING kit.

2. Linearity:

Not applicable, this is a qualitative test.

3. Analytical Specificity/Interference:

This clearance is for the addition of urine to the acceptable matrices for a previously cleared device, where specificity/interference was demonstrated in the original clearance (see K130500).

4. Assay Reportable Range:

Not applicable, this is a qualitative test.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

No reference standards and methods available. Controls are internally manufactured by the manufacturer from myeloma serum samples with representative Immunoglobulin G with kappa light chain (IgGK), Immunoglobulin A with kappa light chain (IgAK), and Immunoglobulin M with lambda light chain (IgML) monoclonal proteins and are validated by both Immunofixation Gel Electrophoresis and Capillary Electrophoresis methods.

Stability: The manufacturer provided data to support real-time stability of two years and on-board stability of two months for the CAPI 3 IMMUNOTYPING Kit.

Sample Stability at 2–8°C

Ten urine samples, including normal and pathological urine samples, were analyzed at the beginning of the study (reference) and after one week storage at 2–8°C (test), with the CAPI 3 IMMUNOTYPING URINE procedure performed with the CAPILLARYS 3 TERA instrument. The results obtained comply with the acceptance criteria defined by SEBIA for the CAPI 3 IMMUNOTYPING URINE procedure performed with the CAPILLARYS 3 TERA instrument. Urine samples can be stored for one week between 2 and 8°C.

Stability –70 /–80°C

Eleven urine samples including normal and pathological urine samples were analyzed at the beginning of the study (reference) and after one month storage at –70 / –80°C (test), with the CAPI 3 IMMUNOTYPING URINE procedure performed with the CAPILLARYS 3 TERA instrument. The results obtained comply with the acceptance criteria defined by SEBIA for the CAPI 3 IMMUNOTYPING URINE procedure performed with the CAPILLARYS 3 TERA instrument. Urine samples can be stored for one month between –70 and –80°C.

6. Detection Limit:

Serial dilutions were prepared in normal urine with three pathological urine samples exhibiting monoclonal components and analyzed using the CAPI 3 IMMUNOTYPING URINE procedure. The results are summarized below:

Sample	Type	Detection Limit mg/dL
1	Lambda Free	1.0
2	Kappa Free	3.0
3	IgG (Lambda)	0.4
	Lambda	0.4

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The method comparison study included 52 urines samples composed of 8 urine samples without monoclonal component and 44 urine samples with monoclonal component including Bence Jones proteins. The samples were tested using the CAPI 3 IMMUNOTYPING URINE procedure performed with the CAPILLARYS 3 TERA instrument (test technique) and the CAPILLARYS IMMUNOTYPING URINE procedure performed with the CAPILLARYS 2 instrument (reference technique). All electropherograms were evaluated visually for the qualitative results. This study demonstrated a 100 % agreement between the two techniques.

Qualitative Results	Number of urine samples	Percent Agreement
IgG Lambda	5	100%
IgG Kappa	2	100%
IgG Lambda with Lambda free	4	100%
IgG Kappa with Kappa free	2	100%
Lambda free	19	100%
Kappa free	8	100%
IgM Kappa with Kappa free	2	100%
IgA Lambda	1	100%
IgA Lambda with Lambda free	1	100%
Without Monoclonal	8	100%
Grand Total	52	100%

2. Matrix Comparison:

Not applicable, the results in urine are not directly comparable to serum.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable, clinical studies were not required for the addition of this matrix.

2. Clinical Specificity:

Not applicable, clinical studies were not required for the addition of this matrix.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

D Clinical Cut-Off:

Not applicable, this is a qualitative test.

E Expected Values/Reference Range:

Absence of monoclonal immunoglobulins in apparently healthy individuals

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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