510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM

A. 510(k) Number:

K161928

B. Purpose for Submission:

Modification to previously cleared devices and previously cleared instrument and renamed as CAPI 3 IMMUNOTYPING using The CAPILLARYS TERA Instrument.

C. Measurand:

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

D. Type of Test:

Capillary Zone Electrophoresis

E. Applicant:

SEBIA, INC.

F. Proprietary and Established Names:

CAPI 3 IMMUNOTYPING, CAPILLARYS 3 TERA, IT/IF Control

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 codes:

   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):

CAPI 3 Immunotyping using CAPILLARYS 3 TERA instrument:
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).

The CAPILLARYS 3 TERA instrument 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 (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 (IgG, IgA, IgM, Kappa and Lambda) with the electrophoresis methods:

- Immunotyping performed using capillary electrophoresis on SEBIA CAPILLARYS 2, CAPILLARYS 2 FLEX-PIERCING and CAPILLARYS 3 TERA 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 CAPILLARYS and 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 to be used with the CAPILLARYS 3 TERA instrument and the IT/IF Control

   The device is for prescription use only.

4. Special instrument requirements:

   For CAPI 3 IMMUNOTYPING KIT: CAPILLARYS 3 TERA instrument

   FOR IT/IF CONTROL:

   - CAPILLARYS 3 TERA instrument
   - CAPILLARYS 2 and CAPILLARYS 2 FLEX-PIERCING cleared in K130500
   - 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:

CAPI 3 IMMUNOTYPING:

CAPI 3 IMMUNOTYPING kit (PN 2600) contains the sample diluent, ELP solution and specific antisera against gamma (IgG), alpha (IgA), mu (IgM) heavy chains, and free and bound Kappa and Lambda light chains.

A sample dilution is prepared and injected at the anodic end of six capillaries. The reference pattern (ELP pattern), which is a complete electrophoretic pattern of the sample's proteins, is obtained by mixing the sample with the ELP solution and injecting it into the first capillary. The antisera patterns are obtained by sample aspiration into the five subsequent capillaries. Separation is performed in a high-voltage electrical field and proteins are detected using absorbance at 200 nm.

The CAPI 3 IMMUNOTYPING kit is designed for the SEBIA CAPILLARYS 3 TERA intrument (PN 1246), a complete automated capillary electrophoresis system.

IT/IF Control:

The IT/IF Control is obtained from a pool of human sera complemented with monoclonal immunoglobulins displaying the five specificities IgG, IgA, IgM, and Kappa and Lambda light chains.
The IT/IF Control is supplied in a stabilized lyophilized form.

J. Substantial Equivalence Information:

1. Predicate device names and 510(k) numbers:

   SEBIA CAPILLARYS IMMUNOTYPING, K130500
   SEBIA CAPILLARYS 2 and CAPILLARYS 2 FLEX-PIERCING Instruments, K130500
   SEBIA IT/IF Control, K130500

2. Comparison with predicate:

   CAPILLARYS IMMUNOTYPING:

Similarities		
Item	CAPI 3 IMMUNOTYPING	CAPILLARYS IMMUNOTYPING
IFE Antisera Specificity	IgG, IgA, IgM heavy chains and Kappa, Lambda light chains	Same
IFE Antisera Storage	2–8ºC	Same
Buffer pH	pH 9.9	Same
Technology	Serum Capillary Electrophoresis: Capillary Electrophoretic Migration with Immunofixation by Subtraction (Immunotyping)	Same
On board stability	Two months	Same
Results	Qualitative Interpretation	Same

Differences		
Item	CAPI 3 IMMUNOTYPING	CAPILLARYS IMMUNOTYPING
Intended use/ Indication for use	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). The CAPILLARYS 3 TERA instrument performs all procedural sequences	The CAPILLARYSIMMUNOTYPING kit is designed for the detection and the 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 CAPILLARYS PROTEIN(E) 6 kit, SEBIA, designed for proteins separation into 6 major fractions in alkaline buffer (pH 9.9). The CAPILLARYS, CAPILLARYS 2 and the CAPILLARYS 2 FLEX-PIERCING perform all procedural

Differences		
Item	CAPI 3 IMMUNOTYPING	CAPILLARYS IMMUNOTYPING
	automatically to obtain a protein profile for qualitative analysis. Each serum sample is mixed with individual antisera that are specific against gamma (IgG), alpha (IgA) and mu (IgM) 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.	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 (IgG), alpha (IgA) and mu (IgM) 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.
Sample type	Serum	Serum and urine
Shelf-life stability	18 months at 2–8ºC	Two months at 2–8ºC
Equipment	Automated CAPILLARYS 3 TERA electrophoresis System	Automated CAPILLARYS 2 or CAPILLARYS 2 Flex-Piercing, electrophoresis System
Detection Limit	IgG Lambda: 30.9 mg/dL IgA Kappa: 13.3 mg/dL IgM Kappa: 25.0 mg/dL	IgG Kappa: 25.0 mg/dL IgA Lambda: 50.0 mg/dL IgM Lambda: 25.0 mg/dL

CAPILLARYS INSTRUMENT:

Similarities		
Item	CAPILLARYS 3 TERA	CAPILLARYS 2 FLEX-PIERCING
Results	Qualitative Monoclonal Protein Interpretation	Same
Temperature control	Peltier device	Same
Software for data processing	SEBIA PHORESIS™ software	Same
Samples tubes	Uncapped tubes or capped tubes depending on the procedure	Same

Differences		
Item	CAPILLARYS 3 TERA	CAPILLARYS 2 FLEX-PIERCING
Intended Use	The CAPILLARYS 3 TERA instrument 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 (IgG), alpha (IgA), and mu (IgM) heavy chains, 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.	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 (IgG), alpha (IgA), and mu (IgM) heavy chains, 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.
Instrument	SEBIA CAPILLARYS 3 TERA, PN 1246	SEBIA CAPILLARYS 2 FLEX-PIERCING instrument, PN 1227 SEBIA CAPILLARYS 2 instrument, PN 1222
Analysis throughput	21 analyses in two hours	16 analyses in two hours
Detection system	Deuterium lamp and LED	Deuterium lamp
Number of separation units	12 parallel capillaries	Eight parallel capillaries
Reagent identification	Yes (RFID labels on reagent vials)	No
Dimensions	L. 90 cm x H. 54 cm x D. 67 cm	L. 95 cm x H. 39 cm x D. 63 cm

IT/IF CONTROL:

Similarities		
Item	IT/IF CONTROL	IT/IF CONTROL
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, CAPILLARYS 2 FLEX-PIERCING and CAPILLARYS 3 TERA 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 CAPILLARYS and 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.	Same
Results	Qualitative Monoclonal Protein Interpretation	Same
Format	One vial (lyophilized; 1.0 mL)	Same
Preparation	Reconstitute the lyophilized control with 1.0 mL distilled or deionized water	Same
Storage temperature	Before reconstitution, the lyophilized control must be stored between 2–8ºC. They are stable until the expiration date indicated on the vial.	Same

Differences		
Item	IT/IF CONTROL	IT/IF CONTROL
Storage stability	Four years at 2–8 ºC	Three years at 2–8 ºC

K. Standard/Guidance Document Referenced:

None Provided.

L. Test Principle:

The CAPILLARYS 3 TERA instrument electrophoresis system uses the principle of capillary electrophoresis in liquid medium. 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. The CAPILLARYS 3 TERA instrument has silica capillaries functioning in parallel allowing 12 simultaneous analyses.

In immunotyping, a sample dilution is prepared and injected at the anodic end of six capillaries. The reference pattern (ELP pattern), which is a complete electrophoretic pattern of the sample's proteins, is obtained by mixing the sample with the ELP solution and injecting it into the first capillary. The antisera patterns are obtained by sample aspiration into the five subsequent capillaries. Previously diluted samples are mixed with specific antisera against gamma (IgG), alpha (IgA), mu (IgM) heavy chains, and free and bound Kappa and Lambda light chains. Protein separation is performed in a high voltage electrical field. The separated proteins are detected using absorbance at 200 nm at the cathodic end of the capillary. After the analysis, the capillaries are immediately washed with a wash solution and filled with buffer which prepares the capillaries for the next analysis.

The immunotyping is performed in four automated steps:

1. Dilution of serum samples with a specific diluent in the pre-dilution well of the reagent cup. This dilution is made according to the sample's immunoglobulin concentration.

2. Mixing diluted serum sample with specific antisera. The antigen-antibody complex is formed rapidly in liquid medium.

3. Injection of the prepared samples with simultaneous aspiration into six capillaries at the anodic end. Protein separation occurs when a high-voltage field is applied to the alkaline buffer. The separated proteins are detected using absorbance at 200 nm at the cathodic end of the capillary

4. Overlay of the ELP pattern on the antisera patterns (IgG, IgA, IgM, Kappa and Lambda light chains) allows the qualitative characterization and result interpretation of suspected monoclonal component.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

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

Within-run and between-capillary precision:

Six different serum samples (five pathological samples with monoclonal proteins and one normal sample) were qualitatively tested 12 times in two runs using the CAPI 3 IMMUNOTYPING on 12 capillaries on the CAPILLARYS 3 TERA instrument. One lot of the CAPI 3 IMMUNOTYPING was used. Each sample was anaylzed with each reagent: ELP solution, anti-IgG, anti-IgA, anti-IgM, anti-kappa and anti-lambda antisera. For each tested reagent, all samples gave concordant results within-run and between-capillaries.

Within-run reproducibility of IT/IF Control:

Three IT/IF control lots were run six times within a run and the run was repeated with three different immunotyping antisera lot numbers on the CAPILLARYS 3 TERA instrument. The IT/IF controls were comprised of one monoclonal IgGL, one IgAL, and one IgMK. According to the identified monoclonal protein, concordant and reproducible within-run results were obtained.

Between-run and between-lot reproducibility of CAPILLARYS 3 IMMUNOTYPING and IT/IF Control on three CAPILLARYS 3 TERA instrument:

Five pathological and one normal serum sample were analyzed three times and repeated in three different runs (with a total of 18 runs) over five working days. The tests were performed with three different CAPILLARYS 3 IMMUNOTYPING kit lot numbers, three different IT/IF Control lots, and three different CAPILLARYS 3 TERA instruments. According to the identified monoclonal protein characterization, concordant and reproducible results were obtained for both pathological and normal serum samples on all lots and instruments.

b. Linearity/assay reportable range:

Not applicable.

c. 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 IgGK, IgAK, and 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 18 months and on-board stability of two months for the CAPI 3 IT Kit.

d. Detection limit:

Limit of detection was performed on three pathological samples: IgA Kappa, IgG Lambda and IgM Kappa with concentration levels of 3.40 g/L, 3.96 g/L and 1.60 g/L, respectively. These three samples were serially diluted at 1:2 down to 1:512 dilution for IgG Lambda and IgM Kappa and down to 1:1024 dilution for IgA Kappa to obtain the variable monoclonal component concentration. The testing was performed on both the Capillarys on Capillarys 2 Flex-Piercing predicate device and CAPI 3 IT on CAP 3 TERA new device. The new device met the acceptance criteria and the Limit of detection results using CAPI 3 IT on CAPILLARY 3 TERA are listed below:

Sample	Type	Dection Limit (mg/L)
1	IgA, Kappa	13.3
2	IgG, Lambda	30.9
3	IgM, Kappa	25.0

e. Analytical specificity:

The Immunotyping interference study was perfomed by testing two samples (normal and pathological) with the interferents. These were tested using the CAPI 3 IT on CAPILLARY 3 TERA instrument. The interferents tested were: hemoglobin, lipids (cholesterol and triglycerides), bilirubin, and rheumatoid factor . No interference was observed in anysample. The results of testing pathological serum samples representing IgGK, IgGL, IgAK, IgAL, IgMK and one normal serum sample are shown in the table below:

Immunotyping Interference Study		
Interferents	**Number samples**	**Results**
Hemoglobin : 0.2 g/dL	Four Pathological: IgA, K (6.4 g/L), IgG, L (7.6 g/L), IgM, K (3.6 g/L), IgM, L (3.4 g/L) and one Normal	No interference
Triglycerides: 3.59 g/dL (41 mM)	Three Pathological: IgA, L (7.2 g/L), IgM, K (16.4 g/L),	No interference

Immunotyping Interference Study		
Interferents	**Number samples**	**Results**
	IgG, K (17.4 g/L) and one Normal	
Bilirubin : 20 mg/dL (342 µM)	Four Pathological: IgG, L (4.8 g/L), IgA, L (1.2 g/L), IgM, K (8.1 g/L), IgM, L (1.8 g/L) and one Normal	No interference
Rheumatoid Factor : 981 IU/mL	Four Pathological: IgA, L (7.2 g/L), IgM, K (16.4 g/L), IgG, K (17.4 g/L), IgA, K (57.2 g/L), IgM, L (3.4 g/L) and one Normal	No interference

Note: The Package Insert Interference and Limitation section states: "A therapeutic monoclonal antibody, such as daratumumab, present in samples from patients with plasma cell discrasia may interfere with the CAPI 3 IMMUNOTYPING procedure, and cites the literature reference: "Monitoring multiple myeloma patients treated with daratumumab: teasing out monoclonal antibody interference - Christopher McCudden et. al., Clin. Chem. Lab. Med. 2016"

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 115 serum samples (103 pathological and 12 normal) were evaluated using the CAPILLARYS IMMUNOTYPING devices on the CAPILLARYS 2 FLEX-PIERCING instrument and the CAPI 3 IMMUNOTYPING devices on the CAPILLARYS 3 TERA instrument. There was 100% agreement between the two methods. The results are presented in the table below:

Sample	N	Percent Agreement Between Devices
Normal	12	100%
IgG Kappa	37	100%
IgG Lambda	27	100%
IgA Kappa	6	100%
IgA Lambda	4	100%
IgM Kappa	14	100%
IgM Lambda	4	100%
2 IgA, Kappa	3	100%
2 IgM, Kappa	2	100%
Kappa free	1	100%
2 Lambda free	1	100%
IgG, Kappa / IgG, Lambda (Biclonal)	2	100%
2 IgA, Kappa/ IgG, Kappa (Triclonal)	1	100%
IgG, Kappa/ IgA, Kappa/ IgM, Lambda (Triclonal)	1	100%
Grand Total	115	100%

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

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 in apparently healthy individuals.

N. Instrument Name:

SEBIA CAPILLARYS 3 TERA

O. System Descriptions:

1. Modes of Operation:

   Closed tube batch mode with the following automated steps:

   a. Bar code reading of sample tubes and sample racks

   b. Sample injection from antisera segments

   c. 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:

   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 CAPI 3 IMMUNOTYPING test using the CAPILLARYS 3 Tera instrument is a modification of a previously cleared CAPILLARYS IT Kit for CAPILLARYS 2 and CAPILLARYS 2 FLEX PIERCING instruments (K103500) which was for the detection and characterization of monoclonal proteins in serum and urine. The SEBIA CAPILLARYS IMMUNOTYPING Kit and SEBIA IT/IF Control (k130500) 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 substantial equivalence decision.