

The Sebia logo is rendered in a bold, lowercase, sans-serif font. The letters are a vibrant green color. The 's' and 'b' are particularly thick and rounded. The logo is positioned in the upper left quadrant of the page, partially overlapping a light green horizontal bar and a light green vertical bar that runs down the left side of the page.

**CAPILLARYS HEMOGLOBIN(E)
USING THE CAPILLARYS 2 FLEX-PIERCING
INSTRUMENT**

2014/06

CAPILLARYS HEMOGLOBIN(E) USING THE CAPILLARYS 2 FLEX-PIERCING INSTRUMENT

INTENDED USE

The CAPILLARYS HEMOGLOBIN(E) kit is designed for the separation of the normal hemoglobins (A, A2 and F) in human blood samples, and for the detection of the major hemoglobin variants (S, C, E and D), by capillary electrophoresis in alkaline buffer (pH 9.4) with the SEBIA CAPILLARYS 2 FLEX-PIERCING instrument. The CAPILLARYS HEMOGLOBIN(E) kit is designed for laboratory use.

The CAPILLARYS 2 FLEX-PIERCING instrument is an automated analyzer which performs a complete hemoglobin profile for the quantitative analysis of the normal hemoglobin fractions A, A2 and F and for the detection of major hemoglobin variants S, C, E and D. The assay is performed on the hemolyse of whole blood samples collected in tubes containing K_2EDTA or K_3EDTA as anticoagulant.

For *In Vitro* Diagnostic Use.

PRINCIPLE OF THE TEST 1-20

Hemoglobin is a complex molecule composed of two pairs of polypeptide chains. Each chain is linked to the heme, a tetrapyrrolic nucleus (porphyrin) which chelates an iron atom. The heme part is common to all hemoglobins and their variants. The type of hemoglobin is determined by the protein part called globin. Polypeptide chains α , β , δ and γ constitute the normal human hemoglobins:

- hemoglobin A = $\alpha_2\beta_2$
- hemoglobin A2 = $\alpha_2\delta_2$
- fetal hemoglobin F = $\alpha_2\gamma_2$

The α -chain is common to these three hemoglobins.

The hemoglobin spatial structure and other molecular properties (like that of all proteins) depend on the nature and the sequence of the amino acids constituting the chains. Substitution of amino acids by mutation is responsible for formation of hemoglobin variants which have different surface charge and consequently different electrophoretic mobilities, which also depend on the pH and ionic strength of the buffer.

The resulting qualitative (or structural) abnormalities are called hemoglobinopathies^(9,10,13). Decreased synthesis of one of the hemoglobin chains leads to quantitative (or regulation) abnormalities, called thalassemias.

Hemoglobin electrophoresis is a well established technique routinely used in clinical laboratories for screening samples for hemoglobin abnormalities^(1,2,3,4,12). The CAPILLARYS 2 FLEX-PIERCING instrument has been developed to provide complete automation of this testing with fast separation and good resolution. In many respects, the methodology can be considered as an intermediary type of technique between classical zone electrophoresis and liquid chromatography^(8,11).

The CAPILLARYS 2 FLEX-PIERCING instrument 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⁽⁵⁾.

The CAPILLARYS 2 FLEX-PIERCING instrument has capillaries functioning in parallel allowing 8 simultaneous analyses for hemoglobin quantification from whole blood sample. A sample dilution with hemolyzing solution is prepared and injected by aspiration at the anodic end of the capillary. A high voltage protein separation is then performed and direct detection of the hemoglobins is made at 415 nm at the cathodic end of the capillary. Before each run, the capillaries are washed with a Wash Solution and prepared for the next analysis with buffer.

The hemoglobins, separated in silica capillaries, are directly and specifically detected at an absorbance wave length of 415 nm which is specific to hemoglobins. The resulting electrophoregrams are evaluated visually for pattern abnormalities.

Direct detection provides accurate relative quantification of individual hemoglobin fraction, with particular interest, such as A2 hemoglobin for β thalassemia diagnostic. In addition, the high resolution of this procedure should allow the identification of hemoglobin variants, in particular, to differentiate hemoglobins S from D, and E from C.

The hemoglobin A2 quantification can also be performed when hemoglobin E is present.

By using alkaline pH buffer, normal and abnormal (or variant) hemoglobins are detected in the following order, from cathode to anode: δA_2 (A2 variant), C, A2/O-Arab, E, S, D, G-Philadelphia, F, A, Hope, Bart's, J, N-Baltimore and H.

The carbonic anhydrase is not visualized on the hemoglobin electrophoretic patterns, this permits to identify hemoglobin A2 variants in this migration zone.



REAGENTS AND MATERIALS SUPPLIED IN THE CAPILLARYS HEMOGLOBIN(E) KIT

REAGENTS REQUIRED BUT NOT SUPPLIED

WARNING: See the safety data sheets.

1. NORMAL Hb A2 CONTROL

Composition

The Normal Hb A2 Control (SEBIA, PN 4778) is obtained from a pool of normal human blood samples. The Normal Hb A2 Control is in a stabilized lyophilized form.

Intended use

The Normal Hb A2 Control is designed for the migration control **before starting a new analysis sequence, after the analyses of 10 successive sample racks and at the end of an analysis sequence**, and for the quality control of human hemoglobin A2 quantification with CAPILLARYS HEMOGLOBIN(E) electrophoresis procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument.

Reconstitute each Normal Hb A2 Control vial with the exact volume of distilled or deionized water, as indicated in the package insert of the Normal Hb A2 Control. Allow to stand for 30 minutes and mix gently (avoid formation of foam).

NOTE: The precision of the reconstitution volume to be maintained is $\pm 1.0\%$.

Migration control:

IMPORTANT: For optimal use of the Normal Hb A2 Control with the CAPILLARYS 2 FLEX-PIERCING instrument, it is necessary to use one specific tube designed for blood controls and its corresponding cap (see "EQUIPMENT AND ACCESSORIES REQUIRED", Tubes and caps for Controls) and to identify this tube with one Normal Hb A2 Control bar code label.

The Normal Hb A2 Control should be used as follows:

- Apply the reconstituted Normal Hb A2 Control in a tube designed for blood control.
- Close the tube with its cap.
- Place a wedge adapter for the blood control tube in position No. 1 on the CAPILLARYS 2 FLEX-PIERCING sample rack No. F0 intended for control blood sample, containing a new green dilution segment.
- Place the tube with Normal Hb A2 Control (identified with the Normal Hb A2 Control bar code label) on the wedge adapter on the sample rack No. F0.
- Start the analysis: Slide the sample rack No. F0 into the CAPILLARYS 2 FLEX-PIERCING instrument, select "Automatic dilution" in the window which appears on the screen and validate.
- **After having changed the analysis buffer vial (even if the lot number is identical) or the technique, after a capillary cleaning sequence with CAPICLEAN, after a software upgrade or after capillaries activation**, perform a second series of analyses with the control, by sliding in again immediately the same sample rack No. F0 with the same dilution segment containing the Normal Hb A2 Control, previously diluted during the first series and an empty tube for control identified with the Normal Hb A2 Control bar code in position No. 1. In the window called "Hb A2 Normal Control" which appears on the screen, select "Manual dilution" and validate.

The results are then automatically considered by the software for the data analysis.

IMPORTANT: The hemoglobin A fraction of the Normal Hb A2 Control must show a minimal optical density (OD) of 0.10. Under this value, the recentering of the electrophoretic pattern will not occur correctly. When analysing samples, the identification of hemoglobin fractions, Hb A, Hb F, Hb A2 and Hb C and also the determination of the migration zone of other variants, may be impossible or wrong (see the paragraph RESULT ANALYSIS).

IMPORTANT: For optimal use of the Normal Hb A2 Control, it is necessary to use one bar code label intended to identify the tube for control which contains the Hb A2 Control (close the tube with its specific cap before using it).

NOTES: For the first use of the "HEMOGLOBIN(E)" analysis program with the CAPILLARYS 2 FLEX-PIERCING instrument or after a prolonged stoppage (over 1 week), it is recommended to perform 3 successive series of analyses with the Normal Hb A2 Control.

After the installation of CAPILLARYS 2 FLEX-PIERCING instrument, during the first sequence of blood sample analysis, a red warning signal will appear if hemoglobin A is absent in one sample (and the recentering of the electrophoretic pattern will not be possible, see paragraph «Result analysis»).

It is then recommended to analyze a blood sample with hemoglobin A on the concerned capillary and to analyze again the sample without hemoglobin A by placing it in a position corresponding to a capillary which has already detected hemoglobin A.

Quality control:

The Normal Hb A2 Control should be used as a normal human blood. After reconstitution, use directly the Normal Hb A2 Control as a blood sample to analyze or as a migration control (applied in a tube for control with its cap, identified with one bar code label, and analyzed with the sample rack No. F0 using the wedge adapter, see paragraph before). It will be automatically diluted with hemolysing solution. It is recommended to include one analysis of Normal Hb A2 Control into each run of samples. The values obtained must fall within the range provided with each batch of Hb A2 Control.

IMPORTANT: For optimal use of the Normal Hb A2 Control placed on a sample rack, it is necessary to use one bar code label intended to identify the tube for control which contains the Hb A2 Control (close the tube with its specific cap before using it and place it on a wedge adapter on the sample rack).

Utilization of a wedge adapter for conical tubes intended for controls:

The wedge adapter is intended to support the conical tubes for blood controls on a sample rack No. F0 or on a rack for samples of the CAPILLARYS 2 FLEX-PIERCING instrument. It presents 2 markers which allow estimating of the volume of blood control available to perform the analysis:

- when the tube is supported by the wedge adapter, the upper marker is located at the top of the wedge adapter and corresponds to a volume of about 250 μL of blood control in the tube. When the volume of blood control reaches this level or is higher, it is sufficient to perform the complete analysis of this blood control with the sample rack No. F0.
- when the tube is supported by the wedge adapter, the lower level is located at the bottom of the crenellations and corresponds to a volume of about 100 μL of blood control in the tube. When the volume of blood control reaches this level or is comprised between the 2 markers of the wedge adapter, it is sufficient to perform one analysis of this blood control on a sample rack.

Storage, stability and signs of deterioration

See the package insert of the Normal Hb A2 Control.

NOTE: For optimal use with the CAPILLARYS 2 FLEX-PIERCING instrument, it is recommended to split the Control into 4 aliquots of 400 μL in microtubes before freezing.

The dilution segment containing the hemolyzed Normal Hb A2 Control may be frozen and stored between $-18\text{ }^{\circ}\text{C}$ and $-22\text{ }^{\circ}\text{C}$. Do not freeze and thaw the dilution segment with hemolyzed Control more than twice.

Do not leave the dilution segment with hemolyzed Control at room temperature.

No test method can provide an absolute assurance of the absence of HIV, hepatitis B and C or other infectious agents. Therefore, handle the Normal Hb A2 Control as a hazardous biological material.

This lot of control blood was found negative on assays approved by FDA or EU equivalent regulatory agency:

- against hepatitis B surface antigen;
- for antibody to HCV;
- for antibody to HIV1 and HIV2.

2. DISTILLED OR DEIONIZED WATER

Use

For rinsing capillaries in automated instrument CAPILLARYS 2 FLEX-PIERCING, SEBIA, for capillary electrophoresis.

It is recommended to use filtered distilled or deionized water (on a filter with a porosity $\leq 0.45 \mu\text{m}$) and with a resistivity higher than 10 Megohms \times cm.

To prevent microbial proliferation, change the water every day.

For optimal operation, add 35 $\mu\text{L/dL}$ of CLEAN PROTECT (SEBIA, PN 2059, 1 vial of 5 mL).

IMPORTANT: Before filling the rinse container, it is recommended to wash it with plenty of distilled or deionized water.

3. CAPICLEAN

Composition

The vial of CAPICLEAN concentrated solution (SEBIA, PN 2058, 25 mL) contains: proteolytic enzymes, surfactants and additives nonhazardous at concentrations used, necessary for optimum performances.

Use

For sample probe cleaning in automated instrument CAPILLARYS 2 FLEX-PIERCING, SEBIA, for capillary electrophoresis, during the CAPICLEAN cleaning sequence.

IMPORTANT :

- When less than 500 samples are analyzed within a week, launch a CAPICLEAN cleaning sequence at least once a week.
- When less than 500 samples are analyzed within a day but more than 500 samples are analyzed within a week, launch a CAPICLEAN cleaning sequence after every 500 analyses.
- When more than 500 samples are analyzed within a day, launch a CAPICLEAN cleaning sequence once a day.

See the instruction sheets of CAPICLEAN, SEBIA.

IMPORTANT: Do not re-use the dilution segment after sample probe cleaning.

Storage, stability and signs of deterioration

Store CAPICLEAN refrigerated (2 - 8 °C). It is stable until the expiration date indicated on the vial label. DO NOT FREEZE.

Precipitate or combined particles in suspension (flocules) may be observed in the CAPICLEAN vial without any adverse effects on its utilization.

Do not dissolve this precipitate or these particles. It is recommended to collect only the supernatant.

4. SODIUM HYPOCHLORITE SOLUTION (for sample probe cleaning)

Preparation

Prepare a sodium hypochlorite solution (2 % to 3 % chloride) by diluting 250 mL 9.6 % chloride concentrated solution to 1 liter with cold distilled or deionized water.

Use

For the sample probe cleaning in the CAPILLARYS 2 FLEX-PIERCING instrument (weekly maintenance in order to eliminate adsorbed proteins from the probe).

See the SEBIA CAPILLARYS 2 FLEX-PIERCING instruction manual.

- Use the sample rack designed for the maintenance (No. 100).
- Place a tube containing 2 mL diluted chlorinated solution previously prepared, in position No. 1 on this sample rack.
- Slide the sample rack No. 100 for maintenance in the CAPILLARYS 2 FLEX-PIERCING instrument.
- In the "MAINTENANCE" window which appears on the screen, select "Launch the probe cleaning (chlorinated sodium hypochlorite solution)" and validate.

Storage, stability and signs of deterioration

Store the working chlorinated solution at room temperature in a closed container, it is stable for 3 months. Avoid storage in sunlight, close to heat and ignition source, and to acids and ammonia.

5. CAPILLARYS / MINICAP WASH SOLUTION

Preparation

Each vial of the stock Wash Solution (SEBIA, PN 2052, 2 vials, 75 mL) should be diluted up to 750 mL with distilled or deionized water.

After dilution, the wash solution contains an alkaline solution pH \approx 12.

Use

For washing the capillaries of CAPILLARYS 2 FLEX-PIERCING. This additional reagent is needed when the number of tests in series is below 40.

IMPORTANT: Before filling the wash solution container, it is recommended to wash the opening of the container, the connector and the tube with plenty of distilled or deionized water to avoid salts deposit.

Storage, stability and signs of deterioration

Store the stock and working wash solutions in closed containers at room temperature or refrigerated.

The stock wash solution is stable until the expiration date indicated on the kit or wash solution vial label.

Working wash solution is stable for 3 months. Discard working wash solution if it changes its appearance, e.g., becomes cloudy due to microbial contamination.

NOTES:

The assays that were performed for the validation of reagents demonstrated that, for the different solutions and using an adapted equipment for the reconstitution volume, a variation of $\pm 5 \%$ on the final volume has no adverse effect on the analysis.

The distilled or deionized water used to reconstitute solutions, must be free of bacterial proliferation and mold (use a filter $\leq 0.45 \mu\text{m}$) and have a resistivity higher than 10 Megohms \times cm.

EQUIPMENT AND ACCESSORIES REQUIRED

1. CAPILLARYS 2 FLEX-PIERCING System SEBIA, PN 1227.
2. Sample racks supplied with CAPILLARYS 2 FLEX-PIERCING.
3. CAPILLARYS 2 FLEX-PIERCING racks for tubes 11 mm, SEBIA, PN 1360, 5 units.
4. Container Kit supplied with CAPILLARYS 2 FLEX-PIERCING: Rinse (to fill with distilled or deionized water), wash solution and waste container.
5. Collection tubes with 13 mm diameter and their corresponding caps (maximal length of tube with cap : 90 mm, maximal diameter of cap : 17 mm) : for example, BD Vacutainer, Terumo Venosafe 5 mL, Greiner Bio-one Vacuette 1, 2, 3 or 4 mL or Sarstedt S-Monovette 4 mL tubes (13 x 75 mm), or collection tubes with 11 mm diameter and their corresponding caps (maximal length of tube with cap : 90 mm, maximal diameter of cap : 17 mm) : for example, Sarstedt S-Monovette 2,7 mL or Kabe Labortechnik Primavette S 2,6 mL tubes (11 x 66 mm), or collection tubes with equivalent dimensions approved for clinical assays.
6. Tubes and caps for Controls, SEBIA, PN 9202 (20 units) or PN 9205 (500 units): conical tubes and their caps to analyze blood controls with the CAPILLARYS 2 FLEX-PIERCING instrument.
7. Wedge adapters for tubes for controls SEBIA, PN 9203, 10 units (or supplied with CAPILLARYS 2 FLEX-PIERCING).
8. Boxes for controls storage, SEBIA, PN 2082: 2 boxes for storage of dilution segments containing hemolyzed Controls.

SAMPLES FOR ANALYSIS

Sample collection and storage

Fresh anticoagulated whole blood samples collected in tubes containing K_2 EDTA or K_3 EDTA as anticoagulant are recommended for analysis. Avoid anticoagulants containing iodoacetate. Blood must be collected according to established procedures used in clinical laboratory testing. Samples may be stored for up to 7 days between 2 and 8 °C.

NOTE: Samples should not be stored at room temperature!

Progressive hemoglobins (Hb) degradation may occur for samples stored between 2 to 8 °C.

When the blood sample is stored for more than 7 days at 2 – 8 °C:

- a weak fraction, corresponding to methemoglobin, appears in the Hb S migration zone,
- when Hb C is present, a fraction corresponding to degraded Hb C appears more anodic than Hb A2 which does not interfere with it (Z(E) zone, see the table in paragraph "Interpretation"),
- when Hb O-Arab is present, a fraction corresponding to degraded Hb O-Arab appears in the Hb S migration zone (Z(S) zone, see the table in paragraph "Interpretation"),
- when Hb E is present, a fraction corresponding to degraded Hb E appears in the Z(D) zone (see the table in paragraph "Interpretation"),
- when Hb S is present, a fraction corresponding to degraded Hb S appears in the Hb F migration zone (Z(F) zone, see the table in paragraph "Interpretation"),
- when Hb A is present, a fraction corresponding to degraded Hb A ("aging fraction" of Hb A) appears more anodic (Z11 zone, see the table in paragraph "Interpretation").

When Hb F is present (in blood samples from newborn babies), a fraction appears in the Hb A migration zone (Z(A) zone, see the table in paragraph "Interpretation") due to the sample degradation.

When stored for more than 10 days, viscous aggregates in red blood cells are observed; it is necessary to discard them before the analysis.

Sample preparation

- Use directly whole blood samples.
- Check that all the tubes contain 1 mL minimum of blood and are perfectly closed.
- **Vortex for 5 seconds blood samples stored at 2 - 8 °C for one week.**

WARNING: The tubes must be closed with their corresponding caps designed for the CAPILLARYS HEMOGLOBIN(E) procedure with the CAPILLARYS 2 FLEX-PIERCING instrument (see EQUIPMENT AND ACCESSORIES REQUIRED).

Particular cases:

Analysis of samples without any Hb A or Hb A2 (these samples are perfectly quantified but not identified by zones):

To identify hemoglobin fractions in a sample without any hemoglobin A or hemoglobin A2, it is recommended to prepare this sample according to the following procedure:

- Vortex for 5 seconds the whole blood sample.
- In a conical tube for control, mix one volume (50 μ L) of whole blood to analyze with one volume (50 μ L) of Normal Hb A2 Control and cap the tube.
- Vortex for 5 seconds.
- Place the tube with a wedge adapter on a sample rack of the CAPILLARYS 2 FLEX-PIERCING instrument.
- Slide the sample rack into the CAPILLARYS 2 FLEX-PIERCING instrument.
- Perform the analysis of this sample according to the standard procedure like a usual blood sample.

The results are then automatically considered by the software for the data analysis.

IMPORTANT: For a sample without any Hb A or Hb A2 prepared according to this procedure, the result obtained with the mixed sample will enable presumptive variant identification due to the positioning of the hemoglobins fractions in the appropriate identification zones. Do not report the relative quantification from the mixed sample result.

The relative quantification of hemoglobins should be reported utilizing the initial, unmixed sample result (without any dilution in the blood control).

Analysis of a sample with an additional fraction in Z(C) migration zone (Hb C migration zone) or Z(A2) migration zone (Hb A2 migration zone):

The presence of a Hb Constant Spring variant may be suspected when a hemoglobin fraction is observed in Z(C) or Z(A2) migration zones. This fraction may also be due to plasmatic proteins from the sample (from a patient with anaemia for example, with a decreased [red blood cells] / [plasma] ratio).

The analysis of red blood cells from the same sample, without plasmatic proteins, will confirm the presence of this variant.

Prepare the sample according to the following procedure:

- Centrifuge the whole blood sample to obtain a red blood cells pellet, discard plasma.
- In a microtube, mix one volume (50 µL) of red blood cells from the sample to analyze with 8 volumes (400 µL) of CAPILLARYS HEMOGLOBIN(E) hemolysing solution.
- Vortex for 5 seconds.
- Apply 100 µL of prepared hemolysate in the wells of a new green dilution segment.
- Place this dilution segment on the sample rack No. F0 of CAPILLARYS 2 FLEX-PIERCING.
- Slide the sample rack into the CAPILLARYS 2 FLEX-PIERCING instrument, select "Sample" with "manual dilution" in the window which appears on the screen and validate.

The results are then automatically considered by the software for the data analysis.

Analysis of samples with volume below 1 mL:

- Vortex for 5 seconds the whole blood sample.
- Apply in a conical tube for control 100 µL of whole blood to analyze and cap the tube.
- Place the tube with a wedge adapter on a sample rack of the CAPILLARYS 2 FLEX-PIERCING instrument.
- Slide the sample rack into the CAPILLARYS 2 FLEX-PIERCING instrument at the beginning of an analysis series.
- Perform the analysis of this sample according to the standard procedure like a usual blood sample.

NOTE: Without any bar code label on the conical tube, the sample cannot be identified.

Samples to avoid

- Avoid coagulated blood samples.
- Avoid aged, improperly stored blood samples; the automated hemolysis of samples may be disturbed by viscous aggregates in red blood cells. Then, degradation products (as artefacts) may affect the electrophoretic pattern.

In these 2 previous cases, aggregates in red blood cells may affect the collection of the sample by the probe.

- Do not analyze directly tubes containing less than 1 mL of blood sample, the analysis should be affected (see particular cases).
- The CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument has not been evaluated in the neonate / newborn population (age range – birth to 28 days). SEBIA does not make any claim for validation of neonatal samples under the age of 28 days and reporting results on such samples is the own responsibility of the biologist. Each laboratory should refer to its internal procedures for validation and reporting patients under the age of 28 days.

NOTE : Collection tubes and centrifugation parameters for biological samples are described in the available documentation on pre-analytical phase for bio-medical analysis (data provided by the tube manufacturers, guides and recommendations on biological sample collection...). Without any indication in the instructions for use on the type of tube to use or on the centrifugation, please refer to this documentation and for the dimensions of tube to use, refer to the SEBIA document "Characteristics of tubes to use according to the instrument". The pre-analytical phase must be performed according to the state of art, the different recommendations, including those provided by the tube manufacturers, and applicable regulations.

PROCEDURE

The CAPILLARYS 2 FLEX-PIERCING instrument is a multiparameter instrument for hemoglobins analysis on parallel capillaries. The hemoglobins assay uses 8 capillaries to run the samples.

The sequence of automated steps is as follows:

- Bar code reading of sample tubes (for up to 8 tubes) and sample racks;
- Mixing of blood samples before analysis;
- Sample hemolysis and dilution from primary tubes into dilution segments;
- Capillary washing;
- Injection of hemolyzed samples;
- Hemoglobin separation and direct detection of the separated hemoglobins on capillaries.

The manual steps include:

- Placement of sample tubes (with caps) in sample racks in positions 1 to 8;
- Placement of new dilution segments in sample-racks;
- Placement of racks on the CAPILLARYS 2 FLEX-PIERCING instrument;
- Removal of sample-racks after analysis.

PLEASE CAREFULLY READ THE CAPILLARYS 2 FLEX-PIERCING INSTRUCTION MANUAL.

I. PREPARATION OF CAPILLARYS ANALYSIS

1. Switch on CAPILLARYS 2 FLEX-PIERCING instrument and computer.
2. Set up the software, enter and the instrument automatically starts.
3. The CAPILLARYS HEMOGLOBIN(E) kit is intended to run with "HEMOGLOBIN(E)" analysis program from the CAPILLARYS 2 FLEX-PIERCING instrument. To select "HEMOGLOBIN(E)" analysis program and place the CAPILLARYS HEMOGLOBIN(E) buffer and hemolyzing solution vials in the instrument, please read carefully the CAPILLARYS 2 FLEX-PIERCING instruction manual.
4. The sample rack contains 8 positions for sample tubes. Place up to 8 capped sample tubes with whole blood on each sample rack (positions 1 to 8); the bar code of each tube must be visible in the openings of the sample rack.
5. Position a new dilution segment on each sample rack. The sample rack will be ejected if the segment is missing.
6. Slide the complete sample carrier(s) into the CAPILLARYS 2 FLEX-PIERCING instrument through the opening in the middle of the instrument. Up to 13 sample racks can be introduced successively and continuously into the instrument. **When analyzing a control blood sample, it is advised to use the sample rack No. F0 intended for control blood sample with specific tubes, caps and the wedge adapter for tubes for controls.**

7. Remove analyzed sample racks from the plate on the left side of the instrument.
8. Take off carefully used dilution segments from the sample rack and discard them.

WARNING: Dilution segments with biological samples have to be handled with care.

DILUTION - MIGRATION - DESCRIPTION OF THE AUTOMATED STEPS

1. Bar codes are read on both sample tubes and sample racks.
2. Mixing of tubes.
3. Samples are diluted in hemolysing solution and the sample probe is rinsed after each sample.
4. Capillaries are washed.
5. Diluted samples are injected into capillaries.
6. Migration is carried out under constant voltage for about 8 minutes and the temperature is controlled by Peltier effect.
7. Hemoglobins are detected directly by scanning at 415 nm and an electrophoretic profile appears on the screen of the instrument.

NOTE: These automated steps described above are applied to the first introduced sample rack. The electrophoretic patterns appear after about 20 minutes from the start of the analysis. For the following sample rack, the first three steps (bar code reading, mixing and sample dilution) are performed during analysis of the previous sample rack.

II. RESULT ANALYSIS

At the end of the analysis, relative quantification of individual hemoglobin fractions is performed automatically and profiles can be analyzed; the hemoglobin fractions, Hb A, Hb F and Hb A2 are automatically identified; the Hb A fraction is adjusted in the middle of the review window. The resulting electrophoregrams are evaluated visually for pattern abnormalities.

The potential positions of the different hemoglobin variants (identified in zones called Z1 to Z15) are shown on the screen of the instrument and indicated on the result ticket. The table in paragraph "Interpretation" shows known variants which may be present in each corresponding zone.

When the software identifies a hemoglobin fraction in a defined zone, the name of this zone is framed.

Patterns are automatically adjusted with regard to Hb A and Hb A2 fractions to facilitate their interpretation:

- when Hb A and/or Hb A2 fractions are not detected on an electrophoretic pattern, a yellow warning signal appears, the adjustment is performed using the position of the Hb A fraction on the two previous patterns obtained with the same capillary; then, there is no fraction identified (except when Hb C is detected: in this case, Hb A2 and Hb C fractions are identified);
- when Hb F is detected on an electrophoretic pattern, without any detection of Hb A, the yellow warning signal does not appear, the adjustment is then performed using the position of the Hb F fraction, and Hb F and/or Hb A and/or Hb A2 fractions are identified;
- when the adjustment is not possible, a red warning signal appears, Hb F and Hb A2 fractions are then not identified (Call SEBIA);
- when optical density (OD) is insufficient on a migration control electrophoretic pattern (obtained with the Normal Hb A2 Control, identified with its bar code label on the sample rack No. 0), a warning message is displayed in order to consider or remove this analysis for the determination of Hb A fraction position. Then, a purple warning signal appears on the review window and Hb A and Hb A2 fractions are not identified.

In all cases, the different migration zones (Z1 to Z15) do not appear neither on the screen of the instrument, nor on the ticket result.

On the electrophoretic pattern, the curves of Hb A2 and Hb C fractions, are calculated and redrawn by fitting with adjustment (or fitted) and are overlaid with the native curve. This display allows the Hb A2 fraction quantification if Hb C is present in the sample.

WARNING: In some cases of hemoglobin C (homozygous) or after a technical problem, the hemoglobins A2 and C are not fitted; these fractions are then under-quantified. It is then recommended to quantify the Hb A2 fraction by using another technique.

PLEASE CAREFULLY READ THE CAPILLARYS 2 FLEX-PIERCING INSTRUCTION MANUAL.

III. END OF ANALYSIS SEQUENCE

At the end of each analysis sequence, the operator must initiate the "shut down" procedure of the CAPILLARYS 2 FLEX-PIERCING instrument in order to store capillaries in optimal conditions.

IV. FILLING OF REAGENT CONTAINERS

The CAPILLARYS 2 FLEX-PIERCING instrument has a reagent automatic control.

IMPORTANT: Please refer to the instructions for replacement of reagent containers respecting color code for vials and connectors.

A message will be displayed when it is necessary to perform one of the following tasks:

- Place a new buffer container and / or;
- Place a new hemolysing solution container and / or;
- Fill the container with working wash solution and / or;
- Fill the container with filtered distilled or deionized water for rinsing capillaries and / or;
- Empty the waste container.

WARNING: Do not use marketed deionized water, such as water for ironing for example (risk of damaging capillaries). Use only water with ultrapure quality, such as injection grade water.

IMPORTANT: Before filling the rinse container, it is recommended to wash it with plenty of distilled or deionized water.

PLEASE CAREFULLY READ THE CAPILLARYS 2 FLEX-PIERCING INSTRUCTION MANUAL.

QUALITY CONTROL

After having changed the analysis buffer lot number or the technique, or after a cleaning sequence with CAPICLEAN, **and before starting a new analysis sequence**, it is necessary to run two analysis sequences with the Normal Hb A2 Control, SEBIA, PN 4778, and the sample rack No. F0 intended for control blood sample (see paragraph REAGENTS REQUIRED BUT NOT SUPPLIED).

It is also advised to include into each run of samples, an assayed control blood (for example, a blood sample containing hemoglobins A, F, C and S, such as Hb AFSC Control, SEBIA, PN 4792, or a normal blood sample, the Normal Hb A2 Control, SEBIA, PN 4778 or the Pathological Hb A2 Control, SEBIA, PN 4779).

IMPORTANT: For optimal use of the blood controls analyzed with the CAPILLARYS 2 FLEX-PIERCING instrument, it is necessary to use the specific conical tubes for controls and their corresponding caps, the wedge adapters for tubes for controls (see EQUIPMENT AND ACCESSORIES REQUIRED) and the bar code labels intended to identify the tubes for controls that contain the blood control to analyze (see the paragraph "Normal Hb A2 Control" for the utilization of a wedge adapter for tubes for controls).

* US customers: Follow federal, state and local guidelines for quality control.

RESULTS

Values

Direct detection at 415 nm in capillaries yields relative concentrations (percentages) of individual hemoglobin zones.

Reference values for individual major electrophoretic hemoglobin zones in the CAPILLARYS 2 FLEX-PIERCING instrument have been established from a healthy population of 113 adults (men and women) with normal hemoglobin values using HPLC technique:

Hemoglobin A: comprised between 96.7 and 97.8 %

Hemoglobin F: ≤ 0.5 % (*)

Hemoglobin A2: comprised between 2.2 and 3.2 %

(*) See Interference and limitations

It is recommended that each laboratory establish its own threshold values.

NOTE: Reference values have been established using the standard parameters of the PHORESIS software (smoothing 0 and hemoglobin fractions automatic quantification with HEMOGLOBIN(E) analysis program).

WARNING: Reference values must be considered only when hemoglobin variants are absent.

Interpretation

See ELECTROPHORETIC PATTERNS, figures 1 – 18.

The different migration zones of hemoglobin variants (called Z1 to Z15) are shown on the screen of the instrument and on the result ticket. Passing the mouse cursor over a zone name displays icon information containing possible hemoglobin variants that could be seen in this zone.

For each fraction, the maximum position defines the migration zone.

See the table showing the potential variants located in each zone.

1. Qualitative abnormalities: Hemoglobinopathies

Most hemoglobinopathies are due to substitution by mutation of a single amino acid in one of the four types of polypeptide chains^(1, 2, 4, 9, 12). The clinical significance of such a change depends on the type of amino acid and the site involved⁽¹³⁾. In clinically significant disease, either the α -chain or the β -chain is affected.

More than 1400 variants of adult hemoglobin have been described^(6, 14). The first abnormal hemoglobins studied and the most frequently occurring have an altered net electric charge, leading to an easy detection by electrophoresis.

There are five main abnormal hemoglobins which present a particular clinical interest: S, C, E, O-Arab and D.

The CAPILLARYS HEMOGLOBIN(E) kit is intended for the identification of hemoglobinopathies and thalassemias.

Hemoglobin S

Hemoglobin S is the most frequent. It is due to the replacement of one glutamic acid (an acidic amino acid No. 6) of the β -chain by valine (a neutral amino acid): when compared to Hb A, its isoelectric point is elevated and its total negative charge decreased with the analysis pH. Its electrophoretic mobility is therefore increased in the capillary and this hemoglobin is faster than A fraction. With alkaline buffered CAPILLARYS HEMOGLOBIN(E) procedure, hemoglobin S migrates between A and A2 fractions, next to Hb A2.

Hemoglobin C

One glutamic acid of the β -chain is replaced by lysine (a basic amino acid No. 6): its mobility is strongly reduced. When compared to Hb A, its isoelectric point is highly elevated and its total negative charge decreased with the analysis pH. Its electrophoretic mobility is therefore increased in the capillary and this hemoglobin is faster than A fraction which allows its differentiation. Hemoglobins C, E and O-Arab are not superimposed on the electrophoretic pattern and are easily identified.

Hemoglobin E

One glutamic acid of the β -chain (No. 26) is replaced by lysine. With CAPILLARYS HEMOGLOBIN(E) procedure, hemoglobin E migrates just anodically behind hemoglobin A2 and is totally separated from it. Then, when hemoglobin E is present, A2 fraction can be measured to detect β thalassemia.

Hemoglobin O-Arab

One glutamic acid of the β -chain (No. 121) is replaced by lysine. With CAPILLARYS HEMOGLOBIN(E) procedure, hemoglobin O-Arab migrates exactly like hemoglobin A2. In such a case, hemoglobin A2 can not be quantified. When this fraction is $> 9\%$, hemoglobin O-Arab must be suspected. Note that Hb O-Arab migrates separately from hemoglobins C and E.

Hemoglobin D (-Los Angeles)

One glutamic acid of the β -chain (No. 121) is replaced by glutamine. With CAPILLARYS HEMOGLOBIN(E) procedure, hemoglobin D (called D-Punjab, D-Los Angeles, D-Chicago or D-Portugal) migrates behind hemoglobin S, this property allows to differentiate S and D hemoglobins.

2. Quantitative abnormalities: Thalassemias

Thalassemias constitute a quite heterogeneous group of genetic disorders characterized by decreased synthesis of one type of the polypeptide chains. The molecular mechanism of this decrease has not been fully described.

There are two types of thalassemia syndromes:

Alpha-thalassemias

They are characterized by the decrease of synthesis of the α -chains, consequently affecting the synthesis of all normal hemoglobins. The excess of synthesis of the β - and γ -chains in relation to α -chains induces the formation of tetrameres without any α -chain:

- hemoglobin Bart's = γ_4 ,
- hemoglobin H = β_4 .

Hemoglobin H presents a low isoelectric point; with CAPILLARYS HEMOGLOBIN(E) procedure, it migrates more anodic than hemoglobin A (and may appear as one or several fractions).

Beta-thalassemias

They are characterized by the decrease of synthesis of the β -chains.

Therefore hemoglobin F and hemoglobin A2 percentages are increased with respect to hemoglobin A and β -chain variants.

With CAPILLARYS HEMOGLOBIN(E) procedure, values obtained for different normal hemoglobin fractions allow the detection of beta thalassemias.

3. Particular cases

- When there is no hemoglobin A in the sample, a small fraction may be observed in its migration zone; this fraction may be acetylated hemoglobin F which represents about 15 to 25 % of hemoglobin F. The CAPILLARYS 2 FLEX-PIERCING instrument can identify this acetylated hemoglobin separately from the hemoglobin A without any confusion.
 - When a small fraction (about 0.5 to 3 %) migrates between hemoglobins F and $\delta A'2$ (A2 variant), a hemoglobin A2 variant may be suspected.
 - When a hemoglobin A2 variant is detected ($\delta A'2$ or any other A2 variant), it is recommended to add its percentage to hemoglobin A2 for a better beta-thalassemia diagnostic.
 - Some hemoglobin variants (such as Hb Camperdown and Hb Okayama) migrate close to Hb A and may not be separated from this hemoglobin.
 - Some hemoglobin variants (such as Hb Porto-Alegre and degraded Hb S) migrate close to Hb F and may not be separated from it.
 - Weak hemoglobin fractions which migrate in zone Z12 are sometimes quantified with imprecision (too asymmetric Hb Bart's, for example). It is thus necessary to delete automatic quantification and then to quantify them manually.
 - Weak fractions may be observed in Z14 and Z15 migration zones. It is then necessary to analyze the hematologic state of the patient and to perform complementary analyses in order to characterize these fractions (artefact or hemoglobin abnormality).
 - When analysing blood samples from newborn babies, Hb A from samples containing Hb F at high concentrations may be disturbed, especially due to the presence of degraded Hb F in its migration zone. The Hb A percentage indicated by the software may be overvalued. In addition, when hemoglobin variants ($> 4\%$, such as Hb S, Hb C, Hb E or Hb D-Punjab) are present in blood samples containing high Hb F levels ($> 60\%$), it is necessary to perform complementary analyses in order to confirm the presence of Hb A.
 - For newborn babies until 6 – 9 months old, it is recommended to analyze many blood samples (collected monthly, for example) in order to check the Hb F concentration. It will allow to verify the decrease of Hb F concentration and the potential presence of a variant. In case of uncertainty, it is advised to confirm by using complementary studies and to analyze parents' blood samples.
 - **Examples with increased hemoglobin F (Hb F) (except for newborn babies):**
 - pregnancy;
 - patients with sickle cell disease, more than 2 years old, with a Hydre[®] (hydroxyurea) treatment and/or transfused and/or producing naturally Hb F increased by compensation;
 - patients, aged more than 2 years old, with HPFH (hereditary persistence of fetal hemoglobin exhibiting 20 to 40 % Hb F for heterozygous patients);
 - patients, more than 2 years old, with leukaemia (with any type), hereditary haemolytic anemia, diabetes, thyroid disease, hyperactivity of bone marrow, multiple myeloma, cancer with metastases.
- For further informations, please refer to: <http://www.answers.com/topic/fetal-hemoglobin-test>
- When analysing blood samples from transfused patients with sickle cell disease, with low Hb A level ($< 10\%$), Hb S fraction may appear shifted from Z(S) zone to Z(D) zone. It is necessary to analyze the hematologic state and to perform complementary studies in order to confirm the presence of Hb S.

Interference and Limitations

- See SAMPLES FOR ANALYSIS.
- Analyze only blood samples contained in collection tubes indicated in the paragraph "EQUIPMENT AND ACCESSORIES REQUIRED" or tubes with equivalent dimensions approved for clinical assays. Call SEBIA technical service for further information on these devices.
- Do not analyze directly tubes containing less than 1 mL of blood sample.
- Avoid aged, improperly stored blood samples; degradation products (or artefacts) may affect the electrophoretic pattern after 7 days storage.
- After 10 days storage, viscous aggregates composed in red blood cells may appear, they must be discarded before analysis.
- When analysing blood samples with a decreased [red blood cells] / [plasma] ratio (from patients with anaemia), a hemoglobin Constant Spring variant may be suspected when a fraction is observed in Z(C) or Z(A2) migration zones. This fraction may be due to plasmatic proteins present in the sample (see § Sample preparation, Particular cases).
- When an abnormal hemoglobin is detected, use other means of identification (e.g., globin chain electrophoresis), or consult or send sample to a specialized laboratory.

IMPORTANT: It is also necessary to analyze the hematologic state, as complementary results.

- The migration of a hemoglobin variant close to Hb A involves an underestimation of Hb A fraction and that of the variant and consequently, an overestimation of Hb A2 fraction. In order to quantify Hb A2 with precision, it is necessary to delete the separate integration of both variants and Hb A, and to quantify these fractions together.
- Some homozygous "S" subjects receive a "Hydrea®" (hydroxyurea) treatment that can induce synthesis of fetal hemoglobin. With CAPILLARYS HEMOGLOBIN(E) procedure, the mobility of the induced hemoglobin F is not different from the physiological hemoglobin F.
- Due to the resolution and sensitivity limits of zone electrophoresis, it is possible that some hemoglobin variants may not be detected with this method.
- The CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument has not been evaluated in the neonate / newborn population (age range – birth to 28 days). SEBIA does not make any claim for validation of neonatal samples under the age of 28 days and reporting results on such samples is the own responsibility of the biologist. Each laboratory should refer to its internal procedures for validation and reporting patients under the age of 28 days.

The common interfering factors with the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument (triglycerides and bilirubin) were evaluated in studies based on the Clinical Laboratory Standards Institute (CLSI - USA) EP7-A2 guideline "Interference Testing in Clinical Chemistry".

The results are summarized below:

- No qualitative or quantitative interference with the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument was detected if bilirubin concentration is equal to or less than 17.9 mg/dL, or 306 $\mu\text{mol/L}$.
- No qualitative or quantitative interference with the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument was detected if triglycerides concentration is equal to or less than 22.34 g/L.

Troubleshooting

Call SEBIA Technical Service of the supplier when the test fails to perform while the instruction for the preparation and storage of materials, and for the procedure were carefully followed.

Kit reagent Safety Data Sheets and information on cleaning and waste disposal, labeling and safety rules applied by SEBIA, packaging for the transportation of biological samples, and instruments cleaning are available on the "INSTRUCTIONS & SAFETY DATA SHEETS" DVD.

PERFORMANCE DATA

Precision

The precision of the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument was evaluated in a study based on the Clinical Laboratory Standards Institute (CLSI - USA) EP5-A2 guideline "Evaluation of Precision Performance of Quantitative Measurements Methods".

The means, standard deviations and coefficients of variation (CV's %) (n = 80) were calculated for percentages (%) of hemoglobin fractions for each sample, using statistical tools recommended by CLSI.

The results obtained with the CAPILLARYS HEMOGLOBIN(E) procedure indicate a very good reproducibility for quantitative analysis for each hemoglobin component. All electrophoregrams were also interpreted visually.

The results presented below have been obtained using the standard parameters of the CAPILLARYS software (smoothing 0 and hemoglobin fractions automatic quantification with HEMOGLOBIN(E) analysis program).

Reproducibility between capillaries from the same instrument

Seven (7) different blood samples were run using the CAPILLARYS HEMOGLOBIN(E) procedure in all capillaries of the same CAPILLARYS 2 FLEX-PIERCING instrument and with 1 lot of CAPILLARYS HEMOGLOBIN(E) kit. The analyzed blood samples included 2 samples with normal Hb A2 level (No. 1 and 5), 2 samples with increased Hb A2 level (No. 2 and 6), 1 sample with low Hb A2 level (No. 3), 1 pathological sample with Hb F and Hb S (No. 4) and 1 sample with increased Hb F level (No. 7). In this study, each blood sample was analyzed on all capillaries from the same instrument, including 40 runs over 20 working days (at 2 different times of the day). Within each run, samples were analyzed in duplicate. The results for Hb A, Hb A2, Hb F and Hb S percentages are summarized in the following tables.

	Sample No. 1	Sample No. 2	Sample No. 3	Sample No. 4	Sample No. 5	Sample No. 6	Sample No. 7
Mean Hb A %	97.2	95.4	98.1	54.9	97.4	93.8	34.3
Within-run reproducibility (CV %)	0.0	0.0	0.0	0.2	0.1	0.1	0.5
Between-run reproducibility (CV %)	0.0	0.0	0.0	0.2	0.0	0.0	0.6
Between-day reproducibility (CV %)	0.0	0.0	0.0	0.1	0.0	0.0	0.9
Total (CV %)	0.0	0.1	0.0	0.4	0.1	0.1	1.2

	Sample No. 1	Sample No. 2	Sample No. 3	Sample No. 4	Sample No. 5	Sample No. 6	Sample No. 7
Mean Hb A2 %	2.8	4.7	1.9	2.8	2.6	6.2	/
Within-run reproducibility (CV %)	1.6	1.0	1.5	1.6	2.6	1.3	/
Between-run reproducibility (CV %)	0.4	0.0	1.2	0.4	0.0	0.6	/
Between-day reproducibility (CV %)	0.1	0.7	0.0	0.6	0.7	0.6	/
Total (CV %)	1.6	1.2	1.9	1.7	2.6	1.6	/

	Sample No. 1	Sample No. 2	Sample No. 3	Sample No. 4	Sample No. 5	Sample No. 6	Sample No. 7
Mean Hb F %	/	/	/	8.3	/	/	65.2
Within-run reproducibility (CV %)	/	/	/	0.7	/	/	0.3
Between-run reproducibility (CV %)	/	/	/	0.8	/	/	0.4
Between-day reproducibility (CV %)	/	/	/	0.3	/	/	0.5
Total (CV %)	/	/	/	1.1	/	/	0.7

	Sample No. 1	Sample No. 2	Sample No. 3	Sample No. 4	Sample No. 5	Sample No. 6	Sample No. 7
Mean Hb S %	/	/	/	33.9	/	/	/
Within-run reproducibility (CV %)	/	/	/	0.4	/	/	/
Between-run reproducibility (CV %)	/	/	/	0.4	/	/	/
Between-day reproducibility (CV %)	/	/	/	0.1	/	/	/
Total (CV %)	/	/	/	0.6	/	/	/

In addition, none of the repeats showed false positive or false negative values.

Reproducibility between lots and instruments

The reproducibility study was conducted using 7 different blood samples that were tested on 3 CAPILLARYS 2 FLEX-PIERCING instruments with 3 lots of CAPILLARYS HEMOGLOBIN(E) kits. The analyzed blood samples included 2 samples with normal Hb A2 level (No. 1 and 5), 2 samples with increased Hb A2 level (No. 2 and 6), 1 sample with low Hb A2 level (No. 3), 1 pathological sample with Hb F and Hb S (No. 4) and 1 sample with increased Hb F level (No. 7). In this study, each blood sample was analyzed on all capillaries from the 3 CAPILLARYS 2 FLEX-PIERCING instruments, including 60 runs over 27 working days (at 2 different times of the day). Within each run, samples were analyzed in duplicate. The following table summarizes the total instrument-reagent C.V. % range for the individual hemoglobin Hb A, Hb A2, Hb F and Hb S fractions tested.

Hemoglobin	Total CV % range
Hb A	0.0 – 2.0
Hb A2	0.0 – 5.5
Hb F	0.2 – 1.3
Hb S	0.4 – 0.7

Linearity

The linearity of the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument was evaluated in a study based on the Clinical Laboratory Standards Institute (CLSI - USA) EP6-A guideline "Evaluation of the Linearity of Quantitative Measurement Procedures: A statistical Approach".

The results for percentages (%) of hemoglobin fractions were analyzed using statistical tools recommended by CLSI.

Hb A2 linearity

One Hb A2 enriched blood sample (containing 13.2 g/dL total hemoglobin with 9.9 % Hb A2) was mixed with a Hb A2 depleted blood sample (containing 13.4 g/dL total hemoglobin with 0.0 % Hb A2) within different proportions and the dilutions were electrophoresed with CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument.

The CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument gave a good linearity for Hb A and Hb A2 within the entire range studied, with a maximum of about 1.3 g/dL for Hb A2 (**between 0.0 and 9.9 % of Hb A2**).

Hb F linearity

One umbilical cord blood sample (containing 12.7 g/dL total hemoglobin with 75.5 % Hb F) was mixed with a normal blood sample (containing 8.8 g/dL total hemoglobin with 0.0 % Hb F) within different proportions and the dilutions were electrophoresed with CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument.

The CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument gave a good linearity for Hb A and Hb F within the entire range studied, with a maximum of about 9.6 g/dL for Hb F (**between 0.0 and 75.5 % of Hb F**).

Hb S linearity

One blood sample with Hb S (containing 6.0 g/dL total hemoglobin with 90.7 % Hb S and 0.0 % Hb A) was mixed with a normal blood sample (containing 9.1 g/dL total hemoglobin with 0.0 % Hb S and 97.5 % Hb A) within different proportions and the dilutions were electrophoresed with CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument.

The CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument gave a good linearity for Hb S within the entire range studied, with a maximum of about 5.4 g/dL for Hb S (**between 0.0 and 90.7 % of Hb S**) and a good linearity for Hb A within the entire range studied, with a maximum of about 8.9 g/dL for Hb A (**between 0.0 and 97.5 % of Hb A**).

Hb C linearity

One blood sample with Hb C (containing 11.5 g/dL total hemoglobin with 33.2 % Hb C) was mixed with a normal blood sample (containing 13.8 g/dL total hemoglobin with 0.0 % Hb C) within different proportions and the dilutions were electrophoresed with CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument.

The CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument gave a good linearity for Hb C within the entire range studied, with a maximum of about 3.8 g/dL for Hb C in the analyzed sample (**between 0.0 and 33.2 % of Hb C**).

Hb D linearity

One blood sample with Hb D (containing 14.3 g/dL total hemoglobin with 40.9 % Hb D) was mixed with a normal blood sample (containing 14.0 g/dL total hemoglobin with 0.0 % Hb D) within different proportions and the dilutions were electrophoresed with CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument.

The CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument gave a good linearity for Hb D within the entire range studied, with a maximum of about 5.8 g/dL for Hb D in the analyzed sample (**between 0.0 and 40.9 % of Hb D**).

Hb E linearity

One blood sample with Hb E (containing 10.8 g/dL total hemoglobin with 96.1 % Hb E) was mixed with a normal blood sample (containing 12.3 g/dL total hemoglobin with 0.0 % Hb E) within different proportions and the dilutions were electrophoresed with CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument.

The CAPILLARYS HEMOGLOBIN(E) procedure performed with CAPILLARYS 2 FLEX-PIERCING instrument gave a good linearity for Hb E within the entire range studied, with a maximum of about 10.4 g/dL for Hb E in the analyzed sample (**between 0.0 and 96.1 % of Hb E**).

Accuracy – Internal correlation

The internal concordance study of the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument was evaluated in a study based on the Clinical Laboratory Standards Institute (CLSI - USA) EP09-A2 guideline "Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (Interim Revision)".

The results for percentages (%) of hemoglobin fractions were analyzed using statistical tools recommended by CLSI.

NOTE: The results presented below have been obtained from 1 internal accuracy study that has been performed in SEBIA facility. The analyzed blood samples and their diagnostic assessment were provided by 11 hospital laboratories in France and USA. The diagnosis was based on a routine HPLC procedure.

The levels of hemoglobin fractions were measured in 56 blood samples, including 20 samples with hemoglobin variants such as hemoglobins S, C, D and E, both by electrophoretic separations obtained with the CAPILLARYS HEMOGLOBIN(E) procedure with the CAPILLARYS 2 FLEX-PIERCING instrument and a commercially available HPLC system for hemoglobins analysis.

The measured values of hemoglobin fractions from both procedures were analyzed by a linear regression statistical procedure. The results of linear regression analysis for Hb A, Hb A2, Hb F and Hb S are tabulated below ($y = \text{CAPILLARYS HEMOGLOBIN(E) with CAPILLARYS 2 FLEX-PIERCING instrument}$):

Hb fraction	Number of samples	Correlation coefficient	y-Intercept	Slope	Range of Hb % values CAPILLARYS HEMOGLOBIN(E) with CAPILLARYS 2 FLEX- PIERCING instrument
Hb A	56	0.996	- 11.42	1.33	21.0 – 98.2
Hb A2	44	0.978	- 0.08	1.13	0.1 – 6.3
Hb F	56	1.000	- 0.38	0.93	0.0 – 79.0
Hb S	8	0.998	0.06	1.07	6.8 – 41.2

All abnormal hemoglobins or abnormal levels of normal hemoglobins detected with the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument were in agreement with the comparative HPLC system. There was no case observed of false positive, i.e., detection of an abnormal band or abnormal level of a normal band where no such abnormality existed.

Accuracy – External correlations

NOTE: The results presented below have been obtained from 2 external accuracy studies that have been performed in 2 hospital laboratories located in the USA. The diagnosis was based on a routine HPLC procedure.

In study No. 1, the levels of hemoglobin fractions were measured in 123 blood samples, including 33 samples with hemoglobin variants such as hemoglobins S, C and E, both by electrophoretic separations obtained with the CAPILLARYS HEMOGLOBIN(E) procedure with the CAPILLARYS 2 FLEX-PIERCING instrument and a commercially available HPLC system for hemoglobins analysis.

The measured values of hemoglobin fractions from both procedures were analyzed by a linear regression statistical procedure. The results of linear regression analysis for Hb A, Hb A2, Hb F, Hb S and Hb C are tabulated below ($y = \text{CAPILLARYS HEMOGLOBIN(E) with CAPILLARYS 2 FLEX-PIERCING instrument}$):

Hb fraction	Number of samples	Correlation coefficient	y-Intercept	Slope	Range of Hb % values CAPILLARYS HEMOGLOBIN(E) with CAPILLARYS 2 FLEX-PIERCING instrument
Hb A	121	0.999	- 1.71	1.14	0.0 – 98.8
Hb A2	93	0.986	- 0.31	1.16	0.9 – 6.5
Hb F	103	0.997	- 0.65	0.97	0.0 – 90.3
Hb S	26	0.998	- 0.10	1.05	14.2 – 54.8
Hb C	5	0.999	- 1.08	1.02	9.7 – 44.7

All abnormal hemoglobins or abnormal levels of normal hemoglobins detected with the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument were in agreement with the comparative HPLC system. There was no case observed of false positive, i.e., detection of an abnormal band or abnormal level of a normal band where no such abnormality existed.

In study No. 2, the levels of hemoglobin fractions were measured in 183 blood samples, including 83 samples with hemoglobin variants such as hemoglobins S, C and D, both by electrophoretic separations obtained with the CAPILLARYS HEMOGLOBIN(E) procedure with the CAPILLARYS 2 FLEX-PIERCING instrument and a commercially available HPLC system for hemoglobins analysis.

The measured values of hemoglobin fractions from both procedures were analyzed by a linear regression statistical procedure. The results of linear regression analysis for Hb A, Hb A2, Hb F, Hb S, Hb C and Hb D are tabulated below (y = CAPILLARYS HEMOGLOBIN(E) with CAPILLARYS 2 FLEX-PIERCING instrument) :

Hb fraction	Number of samples	Correlation coefficient	y-Intercept	Slope	Range of Hb % values CAPILLARYS HEMOGLOBIN(E) with CAPILLARYS 2 FLEX-PIERCING instrument
Hb A	180	0.991	- 1.75	1.13	0.0 – 98.2
Hb A2	113	0.926	- 0.18	1.04	0.4 – 6.0
Hb F	181	0.991	0.11	1.06	0.0 – 98.2
Hb S	67	0.996	0.66	1.00	5.0 – 93.9
Hb C	13	0.996	0.81	0.94	12.5 – 45.7
Hb D	3	0.980	3.04	1.01	34.7 – 40.9

All abnormal hemoglobins or abnormal levels of normal hemoglobins detected with the CAPILLARYS HEMOGLOBIN(E) procedure performed with the CAPILLARYS 2 FLEX-PIERCING instrument were in agreement with the comparative HPLC system. There was no case observed of false positive, i.e., detection of an abnormal band or abnormal level of a normal band where no such abnormality existed.

BIBLIOGRAPHIE / BIBLIOGRAPHY

1. J. Bardakdjian-Michau, J.-L. Dhondt, R. Ducrocq, F. Galactéros, A. Guyard, F.-X. Huchet, A. Lahary, D. Lena-Russo, P. Maboudou, M.-L. North, C. Prehu, A.-M. Soummer, M. Verschelde, H. Wajcman (2003) Bonnes pratiques de l'étude de l'hémoglobine. *Ann. Biol. Clin.*, 61, 401-409.
2. V.F. Fairbanks, ed. (1980) Hémoglobinopathies and thalassemia: Laboratory methods and case studies. Brian C. Decker, New York.
3. F. Galactéros (1986) Thalassémie, drépanocytose et autres hémoglobinopathies. *Techniques et Biologie*, 3, 174-178.
4. JM Hempe, JN Granger and RD Craver (1997) Capillary isoelectric focusing of hemoglobin variants. *Electrophoresis*, 18, 1785-1795.
5. T.H.J. Huisman and J.H.P. Jonxis (1977) The hemoglobinopathies: techniques of identification. Marcel Dekker, New York.
6. Jellum E *et al.* Diagnostic applications of chromatography and capillary electrophoresis. *J. Chromatogr. B*, 689, 155-164 (1997).
7. Joutovsky A, Hadzi-Nesic J and Nardi MA (2004) HPLC retention time as a diagnostic tool for hemoglobin variants and hemoglobinopathies : a study of 60 000 samples in a clinical diagnostic laboratories. *Clin. Chem.*, 50, 10, 1736-1747.
8. J.S. Krauss, P.A. Drew, M.H. Jonah, M. Trinh, S. Shell, L. Black and C.R. Baisden (1986) Densitometry and microchromatography compared for determination of the hemoglobin C and A2 proportions in hemoglobin C and hemoglobin SC disease and in hemoglobin C trait. *Clin. Chem.* 32, 5, 860-863.
9. Landers JP. Clinical Capillary Electrophoresis. *Clin. Chem.*, 41, 495-509 (1995).
10. C. Livingstone (1986) The hemoglobinopathies. Edit. London.-
11. M. Maier-Redelsberger, R. Giro (1989) Diagnostic biologique des maladies de l'hémoglobine. *Feuillets de biologie*, 170.
12. Oda RP *et al.* Capillary electrophoresis as a clinical tool for the analysis of protein in serum and other body fluids. *Electrophoresis*, 18, 1715-1723 (1997).
13. R.G. Schneider (1978) Methods for detection of hemoglobin variants and hemoglobinopathies in the routine clinical laboratory. *CRC Crit. Rev. Clin. Lab. Sci.* 9, 243-271.
14. L. Vovan, D. Lara-Russo, A. Orsini (1985) Diagnostic biologique des hémoglobinoses. *Ann. Pédiat.* 32, 9, 780-789.
15. <http://globin.cse.psu.edu/hbvar/menu.html> : Hbvar : A Database of Human Hemoglobin Variants and Thalassemias.
16. <http://www.isns-neoscreening.org/agenda.htm>.
17. F Boemer, O Ketelslegers, JM Minon, V Bours, R Schoops (2008) Newborn screening for sickle cell disease using tandem mass spectrometry. *Clin. Chem.*, 54, 12, 2036-2041.
18. Lubin BH, Witkowska HE, Kleman K (1991) Laboratory diagnosis of hemoglobinopathies. *Clin. Biochem.*, 24, 363-374.
19. B Gulbis, B Fontaine, F Vertongen, F Cotton (2003) The place of capillary electrophoresis techniques in screening for haemoglobinopathies. *Ann. Clin. Biochem.*, 40, 659-662.
20. Aguilar-Martinez P *et al* (2010) Arbres décisionnels pour le diagnostic et la caractérisation moléculaire des hémoglobinopathies. *Ann. Biol. Clin.*, 68 (4) : 455-464.
21. Wending A. Procédures de diagnostic ou de dépistage : Justification et validité d'un test de diagnostic ou de dépistage-sensibilité-spécificité. *Impact-Internat*, 1986 ; Sept : 93-97.
22. L. Guis, A. Chaumier, V. Le Gall, S. Havrez (Février 2013) Intégration du Capillarys 2 Flex Piercing (Sebia) dans un laboratoire de biologie médicale spécialisée. *Revue Francophone des Laboratoires*, 449, 47 – 56.
23. I. Agouti, F. Merono, N. Bonello-Palot, C. Badens (2013) Analytical evaluation of the Capillarys 2 Flex piercing for routine haemoglobinopathies diagnosis. *Int. Jnl. Lab. Hem.* 35, 217 – 221.
24. S. Altinier, M. Varagnolo, M. Zaninotto, M. Plebani. (2012) Identification and quantification of hemoglobins in whole blood: the analytical and organizational aspects of Capillarys 2 Flex Piercing compared with agarose electrophoresis and HPLC methods. *Clin. Chem. Lab. Med.* DOI 10.1515/cclm-2012-0061.
25. M. Angastiniotis, J.L. Vives Corrons, E.S. Soteriades, A. Eleftheriou (2013) The Impact of Migrations on the Health Services for Rare Diseases in Europe: The Example of Haemoglobin Disorders. *The Scientific World Journal* Volume 2013, Article ID 727905, 10 pages.
26. Nicole Borbely, Lorraine Phelan, Richard Szydlo, *et al.* (2012) Capillary zone electrophoresis for haemoglobinopathy diagnosis. *J. Clin. Pathol.*, doi: 10.1136/jclinpath-2012-200946.
27. F. Cotton *et al.* (2009) Evaluation of an automated capillary electrophoresis system in the screening for hemoglobinopathies. *Clin. Lab.*, 55 : 217 – 221.
28. D. Greene, A.L. Pyle, J.S. Chang, C. Hoke, T. Lorey (2012) Comparison of Sebia Capillarys Flex capillary electrophoresis with the BioRad Variant II high pressure liquid chromatography in the evaluation of hemoglobinopathies. *Clin. Chim. Acta* 413, 1232 – 1238.
29. T. Higgins, M. Mack, A. Khajuria (2009) Comparison of two methods for the quantification and identification of hemoglobin variants. *Clin. Biochem.*, 42, 701 – 705.
30. D.F. Keren *et al* (2008) Comparison of Sebia Capillarys capillary electrophoresis with the Primus High-Pressure Liquid Chromatography in the evaluation of hemoglobinopathies. *Am. J. Clin. Pathol.*, 130 : 824 – 831.
31. D.F. Keren *et al* (2012) Expression of hemoglobin variant migration by capillary electrophoresis relative to Hemoglobin A2 improves precision. *Am. J. Clin. Pathol.*, 137 : 660 – 664.
32. Can Liao, Jian-Ying Zhou, Xing-Mei Xie, Jian Li, Ru Li, and Dong-Zhi Li (2010). Detection of Hb constant spring by a capillary electrophoresis method. *Hemoglobin*, 34 (2) : 175 – 178.
33. D.M. Mais *et al* (2009) The range of hemoglobin A2 in hemoglobin E heterozygotes as determined by capillary electrophoresis. *Am. J. Clin. Pathol.*, 132 : 34 – 38.
34. T. Munkongdee *et al* (2010) Quantitative analysis of Hb Bart's in cord blood by capillary electrophoresis system. *Ann. Hematol.* DOI 10.1007/s00277-010-1137-4.
35. R. Paleari, B. Gulbis, F. Cotton, A. Mosca (2012) Interlaboratory comparison of current high-performance methods for HbA2. *Int. Jnl. Lab. Hem.* 34, 362 – 368.
36. S. Sangkitporn *et al* (2011) Multicenter validation of fully automated capillary electrophoresis method for diagnosis of thalassemias and hemoglobinopathies in Thailand. *Southeast Asian J. Trop. Med. Public Health* 42 (5), 1224 – 1232.
37. F. Wolff, F. Cotton, B. Gulbis (2012) Screening for haemoglobinopathies on cord blood : laboratory and clinical experience. *J. Med. Screen.*, 19, 3, 116 - 122.

TABLEAU / TABLE

CAPILLARYS HEMOGLOBIN(E) : VARIANTS POTENTIELS PRÉSENTS DANS CHAQUE ZONE
POTENTIAL VARIANTS LOCATED IN EACH ZONE

Zone	Hémoglobines / Hemoglobins (Hb)
Z1	Hb Santa Ana (pic mineur), Hb Mizuho (pic mineur), Hb delta A'2, Hb S-Oman, Hb T-Cambodia, Hb Poissy (pic mineur), variant de Hb A2 "Savaria", variant de Hb A2 "Chad", variant de Hb A2 "Arya", variant de Hb A2 "Hasharon", variant de Hb A2 "Fort de France", variant de Hb A2 "Ottawa", variant de Hb A2 "Shimonoseki", variant de Hb A2 "Russ" (alpha 1), variant de Hb A2 "Matsue-Oki", variant de Hb A2 "Reims", variant de Hb A2 "Mizushi", variant de Hb A2 "Stanleyville-II", variant de Hb A2 "O-Indonesie", variant de Hb A2 "San Antonio", variant de Hb A2 "G-Audhali", variant de Hb A2 "Handsworth", variant de Hb A2 "G-Philadelphie", variant de Hb A2 "Memphis", variant de Hb A2 "Q-Iran", variant de Hb A2 "G-Waimanalo", variant de Hb A2 "Russ" (alpha 2), variant de Hb A2 "Ube-4", variant de Hb A2 "Q-India", variant de Hb A2 "Watts", variant de Hb A2 "Spanish Town", variant de Hb A2 "Montgomery", variant de Hb A2 "G-Norfolk" (alpha 1), variant de Hb A2 "Inkster", variant de Hb A2 "G-Pest", variant de Hb A2 "Winnipeg", variant de Hb A2 "Queens", variant de Hb A2 "Etobicoke", variant de Hb A2 "Chapel Hill", variant de Hb A2 "Park Ridge", variant de Hb A2 "Q-Thailand", variant de Hb A2 "Delfzicht"
	<i>Hb Santa Ana (minor peak), Hb Mizuho (minor peak), Hb delta A'2, Hb S-Oman, Hb T-Cambodia, Hb Poissy (minor peak), "Savaria" Hb A2 variant, "Chad" Hb A2 variant, "Arya" Hb A2 variant, "Hasharon" Hb A2 variant, "Fort de France" Hb A2 variant, "Ottawa" Hb A2 variant, "Shimonoseki" Hb A2 variant, "Russ" Hb A2 variant (alpha 1), "Matsue-Oki" Hb A2 variant, "Reims" Hb A2 variant, "Mizushi" Hb A2 variant, "Stanleyville-II" Hb A2 variant, "O-Indonesie" Hb A2 variant, "San Antonio" Hb A2 variant, "G-Audhali" Hb A2 variant, "Handsworth" Hb A2 variant, "G-Philadelphie" Hb A2 variant, "Memphis" Hb A2 variant, "Q-Iran" Hb A2 variant, "G-Waimanalo" Hb A2 variant, "Russ" Hb A2 variant (alpha 2), "Ube-4" Hb A2 variant, "Q-India" Hb A2 variant, "Watts" Hb A2 variant, "Spanish Town" Hb A2 variant, "Montgomery" Hb A2 variant, "G-Norfolk" Hb A2 variant (alpha 1), "Inkster" Hb A2 variant, "G-Pest" Hb A2 variant, "Winnipeg" Hb A2 variant, "Queens" Hb A2 variant, "Etobicoke" Hb A2 variant, "Chapel Hill" Hb A2 variant, "Park Ridge" Hb A2 variant, "Q-Thailand" Hb A2 variant, "Delfzicht" Hb A2 variant</i>
Z(C)	Hb C-Ziguinchor, Hb F-Hull, Hb F-Texas-I, Hb Constant Spring, Hb C, Hb C-Harlem (C-Georgetown), variant de Hb A2 "Les Lilas", variant de Hb A2 "Boumerdes", variant de Hb A2 "Dunn", variant de Hb A2 "Bassett", variant de Hb A2 "Tarrant", variant de Hb A2 "Sassari", variant de Hb A2 "St. Luke's", variant de Hb A2 "Verdun", variant de Hb A2 "Manitoba-I", variant de Hb A2 "Setif", variant de Hb A2 "Sunshine Seth", variant de Hb A2 "Titusville", variant de Hb A2 "Swan River", variant de Hb A2 "Manitoba-II", variant de Hb A2 "Val de Marne"
	<i>Hb C-Ziguinchor, Hb F-Hull, Hb F-Texas-I, Hb Constant Spring, Hb C, Hb C-Harlem (C-Georgetown), "Les Lilas" Hb A2 variant, "Boumerdes" Hb A2 variant, "Dunn" Hb A2 variant, "Bassett" Hb A2 variant, "Tarrant" Hb A2 variant, "Sassari" Hb A2 variant, "St. Luke's" Hb A2 variant, "Verdun" Hb A2 variant, "Manitoba-I" Hb A2 variant, "Setif" Hb A2 variant, "Sunshine Seth" Hb A2 variant, "Titusville" Hb A2 variant, "Swan River" Hb A2 variant, "Manitoba-II" Hb A2 variant, "Val de Marne" Hb A2 variant</i>
Z(A2)	Hb A2, Hb Chad (E-Keelung), Hb Hong Kong (cas anti-Lepore), Hb O-Tibesti, Hb O-Arab, Hb E-Saskatoon, variant de Hb A2 "Charolles", variant de Hb A2 "Roubaix", variant de Hb A2 "Dallas", variant de Hb A2 "Aztec", variant de Hb A2 "Boghé", variant de Hb A2 "Kosovo", variant de Hb A2 "Bonn", variant de Hb A2 "Brugg", variant de Hb A2 "Buffalo", variant de Hb A2 "Chicago", variant de Hb A2 "Columbia Missouri", variant de Hb A2 "Conakry", variant de Hb A2 "Fontainebleau", variant de Hb A2 "Frankfurt", variant de Hb A2 "Godavari", variant de Hb A2 "Gouda", variant de Hb A2 "Groene Hart", variant de Hb A2 "Hekinan", variant de Hb A2 "Kosovo", variant de Hb A2 "Le Lamentin", variant de Hb A2 "Le Lamentin 2", variant de Hb A2 "Lisbon", variant de Hb A2 "Lyon-Bron", variant de Hb A2 "M-Boston", variant de Hb A2 "Milledgeville", variant de Hb A2 "Mosella", variant de Hb A2 "Noko", variant de Hb A2 "Owari", variant de Hb A2 "Ozieri", variant de Hb A2 "Riccarton", variant de Hb A2 "Rouen", variant de Hb A2 "Saclay", variant de Hb A2 "Taybe", variant de Hb A2 "Toulon", variant de Hb A2 "Twin Peaks", variant de Hb A2 "Verona", variant de Hb A2 "Westmead", variant de Hb A2 "Zoetermeer", variant de Hb A2 "Melusine", variant de Hb A2 "Jura", variant de Hb A2 "Nouakchott"
	<i>Hb A2, Hb Chad (E-Keelung), Hb Hong Kong (anti-Lepore case), Hb O-Tibesti, Hb O-Arab, Hb E-Saskatoon, "Charolles" Hb A2 variant, "Roubaix" Hb A2 variant, "Dallas" Hb A2 variant, "Aztec" Hb A2 variant, "Boghé" Hb A2 variant, "Bonn" Hb A2 variant, "Kosovo" Hb A2 variant, "Brugg" Hb A2 variant, "Buffalo" Hb A2 variant, "Chicago" Hb A2 variant, "Columbia Missouri" Hb A2 variant, "Conakry" Hb A2 variant, "Fontainebleau" Hb A2 variant, "Frankfurt" Hb A2 variant, "Godavari" Hb A2 variant, "Gouda" Hb A2 variant, "Groene Hart" Hb A2 variant, "Hekinan" Hb A2 variant, "Kosovo" Hb A2 variant, "Le Lamentin" Hb A2 variant, "Le Lamentin 2" Hb A2 variant, "Lisbon" Hb A2 variant, "Lyon-Bron" Hb A2 variant, "M-Boston" Hb A2 variant, "Milledgeville" Hb A2 variant, "Mosella" Hb A2 variant, "Noko" Hb A2 variant, "Owari" Hb A2 variant, "Ozieri" Hb A2 variant, "Riccarton" Hb A2 variant, "Rouen" Hb A2 variant, "Saclay" Hb A2 variant, "Taybe" Hb A2 variant, "Toulon" Hb A2 variant, "Twin Peaks" Hb A2 variant, "Verona" Hb A2 variant, "Westmead" Hb A2 variant, "Zoetermeer" Hb A2 variant, "Melusine" Hb A2 variant, "Jura" Hb A2 variant, "Nouakchott" Hb A2 variant</i>
Z(E)	Hb Seal Rock, Hb Köln (Ube-1), Hb Buenos Aires (pic mineur), Hb E, Hb M-Saskatoon (pic mineur), Hb G-Siriraj, Hb A2-Babinga, Hb F-Moyen Orient, Hb Agenogi, Hb Sabine, Hb Santa Ana, Hb Savaria, Hb Djelfa (pic 3), variant de Hb A2 "M-Iwate", variant de Hb A2 "Saint Claude", variant de Hb A2 "Jackson" (alpha 2), variant de Hb A2 "Wayne" (pic 1), Hb C dégradée
	<i>Hb Seal Rock, Hb Köln (Ube-1), Hb Buenos Aires (minor peak), Hb E, Hb M-Saskatoon (minor peak), Hb G-Siriraj, Hb A2-Babinga, Hb F-Moyen Orient, Hb Agenogi, Hb Sabine, Hb Santa Ana, Hb Savaria, Hb Djelfa (peak 3), "M-Iwate" Hb A2 variant, "Saint Claude" Hb A2 variant, "Jackson" Hb A2 variant (alpha 2), "Wayne" Hb A2 variant (peak 1), denatured Hb C</i>

TABLEAU / TABLE

CAPILLARYS HEMOGLOBIN(E) : VARIANTS POTENTIELS PRÉSENTS DANS CHAQUE ZONE
POTENTIAL VARIANTS LOCATED IN EACH ZONE

Zone	Hémoglobines / Hemoglobins (Hb)
Z(S)	<p>Hb Arya, Hb Kenya (HPFH-7), Hb Hasharon (Sinai), Hb Dhofar (Yukuhashi), Hb Shimonoseki (Hikoshima), Hb O-Indonesia (Buginese-X), Hb Machida, Hb Vexin, Hb Corbeil, Hb Ottawa (Siam), Hb Fort de France, Hb S, Hb Montgomery, Hb G-Copenhague, Hb S-Antilles, Hb Handsworth, Hb Poissy, Hb Hamadan, Hb Belfast, Hb Russ (alpha 1), Hb Russ (alpha 2), Hb Evanston, Hb Stanleyville-II, Hb Cocody, Hb Reims, variant de Hb A2 "Tokoname", variant de Hb A2 "Pisa", variant de Hb A2 "Lombard", variant de Hb A2 "Tatras", variant de Hb A2 "J-Cape Town" (alpha 2), variant de Hb A2 "Thionville", variant de Hb A2 "Cemenelum", variant de Hb A2 "J-Cape Town" (alpha 1), variant de Hb A2 "Nikaia", variant de Hb A2 "Hopkins-II" (alpha 1), variant de Hb A2 "Jackson" (alpha 1), variant de Hb A2 "Hopkins-II" (alpha 2), variant de Hb A2 "Singapore", Hb O-Arab dégradée</p> <p><i>Hb Arya, Hb Kenya (HPFH-7), Hb Hasharon (Sinai), Hb Dhofar (Yukuhashi), Hb Shimonoseki (Hikoshima), Hb O-Indonesia (Buginese-X), Hb Machida, Hb Vexin, Hb Corbeil, Hb Ottawa (Siam), Hb Fort de France, Hb S, Hb Montgomery, Hb G-Copenhague, Hb S-Antilles, Hb Handsworth, Hb Poissy, Hb Hamadan, Hb Belfast, Hb Russ (alpha 1), Hb Russ (alpha 2), Hb Evanston, Hb Stanleyville-II, Hb Cocody, Hb Reims, "Tokoname" Hb A2 variant, "Pisa" Hb A2 variant, "Lombard" Hb A2 variant, "Tatras" Hb A2 variant, "J-Cape Town" Hb A2 variant (alpha 2), "Thionville" Hb A2 variant, "Cemenelum" Hb A2 variant, "J-Cape Town" Hb A2 variant (alpha 1), "Nikaia" Hb A2 variant, "Hopkins-II" Hb A2 variant (alpha 1), "Jackson" Hb A2 variant (alpha 1), "Hopkins-II" Hb A2 variant (alpha 2), "Singapore" Hb A2 variant, denatured Hb O-Arab</i></p>
Z(D)	<p>Hb Memphis, Hb G-Audhali, Hb G-Szuhu (Gifu), Hb Leiden, Hb Beograd (D-Camperdown), Hb Muravera, Hb D-Bushman, Hb Matsue-Okii, Hb D-Punjab (D-Los Angeles), Hb Osu Christiansborg, Hb Watts, Hb A2-Coburg, Hb G-Waimanalo (Aida), Hb Muskegon, Hb D-Ibadan, Hb Buenos Aires (pic mineur), Hb Q-India, Hb Lepore-BW, Hb Q-Iran, Hb Summer Hill, Hb G-Philadelphia, Hb D-Ouled Rabah, Hb Yaizu, Hb Kenitra, Hb San Antonio, Hb Ferrara, Hb Lepore-Hollandia, Hb Quin-Hai, Hb Fort Worth, Hb Mizushi, Hb Lepore-Baltimore, Hb Djelfa (pic 2), Hb Spanish Town, Hb Korle-Bu (G-Accra), Hb Köln (Ube-1), Hb G-Norfolk (alpha 1), Hb Maputo, Hb Etobicoke, Hb D-Iran, Hb G-Taïpei, Hb Caribbean, Hb Ube-4, Hb St. Luke's, Hb G-Coushatta (G-Saskatoon), Hb Winnipeg, Hb Inker, Hb Zürich, Hb G-Pest, Hb P-Galveston, Hb Queens (Ogi), Hb Aubenas, Hb Setif, Hb P-Nilotic, Hb Sunshine Seth, Hb Titusville, variant de Hb A2 "J-Sardagna", variant de Hb A2 "Suresnes", variant de Hb A2 "J-Meerut" (alpha 2), variant de Hb A2 "J-Broussais" (alpha 2), variant de Hb A2 "J-Rajappen", variant de Hb A2 "J-Anatolia", variant de Hb A2 "J-Oxford", variant de Hb A2 "J-Meerut" (alpha 1), variant de Hb A2 "Ube-2", variant de Hb A2 "J-Broussais" (alpha 1), variant de Hb A2 "J-Abidjan", variant de Hb A2 "J-Toronto", variant de Hb A2 "Mexico" (alpha 1), variant de Hb A2 "Mexico" (alpha 2), variant de Hb A2 "Thailand", variant de Hb A2 "J-Tongariki", variant de Hb A2 "Neully-sur-Marne", variant de Hb A2 "J-Wenchang-Wuming", variant de Hb A2 "J-Paris-I" (alpha 2), variant de Hb A2 "J-Habana", variant de Hb A2 "J-Paris-I" (alpha 1), variant de Hb A2 "Wayne" (pic 2), Hb E dégradée</p> <p><i>Hb Memphis, Hb G-Audhali, Hb G-Szuhu (Gifu), Hb Leiden, Hb Beograd (D-Camperdown), Hb Muravera, Hb D-Bushman, Hb Matsue-Okii, Hb D-Punjab (D-Los Angeles), Hb Osu Christiansborg, Hb Watts, Hb A2-Coburg, Hb G-Waimanalo (Aida), Hb Muskegon, Hb D-Ibadan, Hb Buenos Aires (minor peak), Hb Q-India, Hb Lepore-BW, Hb Q-Iran, Hb Summer Hill, Hb G-Philadelphia, Hb D-Ouled Rabah, Hb Yaizu, Hb Kenitra, Hb San Antonio, Hb Ferrara, Hb Lepore-Hollandia, Hb Quin-Hai, Hb Fort Worth, Hb Mizushi, Hb Lepore-Baltimore, Hb Djelfa (peak 2), Hb Spanish Town, Hb Korle-Bu (G-Accra), Hb Köln (Ube-1), Hb G-Norfolk (alpha 1), Hb Maputo, Hb Etobicoke, Hb D-Iran, Hb G-Taïpei, Hb Caribbean, Hb Ube-4, Hb St. Luke's, Hb G-Coushatta (G-Saskatoon), Hb Winnipeg, Hb Inker, Hb Zürich, Hb G-Pest, Hb P-Galveston, Hb Queens (Ogi), Hb Aubenas, Hb Setif, Hb P-Nilotic, Hb Sunshine Seth, Hb Titusville, "J-Sardagna" Hb A2 variant, "Suresnes" Hb A2 variant, "J-Meerut" Hb A2 variant (alpha 2), "J-Broussais" Hb A2 variant (alpha 2), "J-Rajappen" Hb A2 variant, "J-Anatolia" Hb A2 variant, "J-Oxford" Hb A2 variant, "J-Meerut" Hb A2 variant (alpha 1), "Ube-2" Hb A2 variant, "J-Broussais" Hb A2 variant (alpha 1), "J-Abidjan" Hb A2 variant, "J-Toronto" Hb A2 variant, "Mexico" Hb A2 variant (alpha 1), "Mexico" Hb A2 variant (alpha 2), "Thailand" Hb A2 variant, "J-Tongariki" Hb A2 variant, "Neully-sur-Marne" Hb A2 variant, "J-Wenchang-Wuming" Hb A2 variant, "J-Paris-I" Hb A2 variant (alpha 2), "J-Habana" Hb A2 variant, "J-Paris-I" Hb A2 variant (alpha 1), "Wayne" Hb A2 variant (peak 2), denatured Hb E</i></p>
Z(F)	<p>Hb F, Hb Willamette, Hb Hoshida, Hb Linguicid, Hb Sunnybrook, Hb Park Ridge, Hb Delfzicht, Hb Alabama, Hb Chapel Hill, Hb Bunbury, Hb Tak, Hb Q-Thailand (G-Taichung), Hb Sabine, Hb Bassett, Hb Les Lilas, Hb Rampa, Hb G-Georgia, Hb Barcelona, Hb G-San José, Hb Denmark Hill, Hb Pôrto Alegre, Hb Geldrop Santa Anna, Hb Ta-Li, Hb Richmond, Hb Abruzzo, Hb Verdun, Hb Boumerdes, Hb Swan River, Hb Burke, Hb Tarrant, Hb Dunn, Hb Manitoba-I, Hb Manitoba-II, Hb Sassari, Hb Hazebrouck, Hb Port Phillip, variant de Hb A2 "J-Rovigo", Hb S dégradée, Hb D-Punjab dégradée</p> <p><i>Hb F, Hb Willamette, Hb Hoshida, Hb Linguicid, Hb Sunnybrook, Hb Park Ridge, Hb Delfzicht, Hb Alabama, Hb Chapel Hill, Hb Bunbury, Hb Tak, Hb Q-Thailand (G-Taichung), Hb Sabine, Hb Bassett, Hb Les Lilas, Hb Rampa, Hb G-Georgia, Hb Barcelona, Hb G-San José, Hb Denmark Hill, Hb Pôrto Alegre, Hb Geldrop Santa Anna, Hb Ta-Li, Hb Richmond, Hb Abruzzo, Hb Verdun, Hb Boumerdes, Hb Swan River, Hb Burke, Hb Tarrant, Hb Dunn, Hb Manitoba-I, Hb Manitoba-II, Hb Sassari, Hb Hazebrouck, Hb Port Phillip, "J-Rovigo" Hb A2 variant, denatured Hb S, denatured Hb D-Punjab</i></p>
Z8	<p>Hb F acétylée, Hb Lansing, Hb Hinsdale, Hb Roanne, Hb Yakima, Hb Ypsilanti (Ypsi - pic 1), Hb Saint Mandé, Hb Alberta, Hb Bruxelles, Hb Val de Marne (Footscray), Hb Kempsey, Hb Shelby (Leslie), Hb Atlanta, Hb Chemilly, Hb S-Clichy, Hb Sarrebourg, Hb Charolles, Hb Ypsilanti (Ypsi - pic 2), Hb Rainier, Hb Athens-GA (Waco), Hb Debrousse, Hb Köln (Ube-1), Hb Aubagne</p> <p><i>Acetylated Hb F, Hb Lansing, Hb Hinsdale, Hb Roanne, Hb Yakima, Hb Ypsilanti (Ypsi - peak 1), Hb Saint Mandé, Hb Alberta, Hb Bruxelles, Hb Val de Marne (Footscray), Hb Kempsey, Hb Shelby (Leslie), Hb Atlanta, Hb Chemilly, Hb S-Clichy, Hb Sarrebourg, Hb Charolles, Hb Ypsilanti (Ypsi - peak 2), Hb Rainier, Hb Athens-GA (Waco), Hb Debrousse, Hb Köln (Ube-1), Hb Aubagne</i></p>

TABLEAU / TABLE

CAPILLARYS HEMOGLOBIN(E) : VARIANTS POTENTIELS PRÉSENTS DANS CHAQUE ZONE
POTENTIAL VARIANTS LOCATED IN EACH ZONE

Zone	Hémoglobines / Hemoglobins (Hb)
Z(A)	<p>Hb A, Hb Presbyterian, Hb Roubaix (Poland), Hb Silver Springs, Hb El Escorial *, Hb Dallas *, Hb Olympia *, Hb Phnom Penh *, Hb La Corona *, Hb Uzes *, Hb Bougardirey-Mail *, Hb Saint Nazaire *, Hb Alzette *, Hb Antibes-Juan-Les-Pins *, Hb Arta (pic majeur) *, Hb Austin *, Hb Aztec *, Hb Beirut *, Hb Bethesda *, Hb Boghé *, Hb Bonn *, Hb Brem-sur-Mer *, Hb Brest *, Hb Brigham *, Hb Brisbane (Great Lakes) *, Hb Brugg *, Hb Buenos Aires (Bryn Mawr - pic majeur) *, Hb Buffalo (Reeuwijk) *, Hb Bushwick *, Hb Chicago *, Hb City of Hope *, Hb Coimbra (Ingelheim) *, Hb Columbia Missouri *, Hb Conakry *, Hb Djelfa (pic 1) *, Hb Fontainebleau *, Hb Frankfurt *, Hb Fukuoka *, Hb Godavari *, Hb Gorwihl (Hinchingsbrooke) *, Hb Gouda *, Hb Grange Blanche *, Hb Groene Hart (Bernalda) *, Hb Hamilton *, Hb Heathrow *, Hb Hekinan *, Hb Iraq-Halabja *, Hb Kosovo *, Hb La Desirade *, Hb Le Lamentin *, Hb Le Lamentin 2 *, Hb Linköping (Meilahti) *, Hb Lisbon *, Hb Little Rock *, Hb Lulu Island *, Hb Lyon-Bron *, Hb M-Boston (M-Osaka) *, Hb M-Saskatoon (pic majeur) *, Hb McKees Rocks *, Hb Malmö *, Hb Marseille (Long Island) *, Hb Milledgeville *, Hb Minneapolis Laos *, Hb Mizuho *, Hb Mosella *, Hb Noko *, Hb Okayama *, Hb Owari *, Hb Ozieri *, Hb Perth (Abraham Lincoln) *, Hb Potomac *, Hb Puttelange *, Hb Raleigh *, Hb Ravenscourt Park *, Hb Regina *, Hb Rhode Island (Southwark) *, Hb Riccarton *, Hb Rouen (Ethiopia) *, Hb Saclay *, Hb St Joseph's *, Hb San Diego *, Hb Santa Juana (Serres) *, Hb Savannah *, Hb Sydney *, Hb Taybe *, Hb Templeuve *, Hb Toulon *, Hb Twin Peaks *, Hb Ty Gard *, Hb Valletta *, Hb Verona *, Hb Villejuif *, Hb Villeparisis *, Hb Volga (Drenthe) *, Hb Westmead *, Hb Wood *, Hb Yaounde (Mataro) *, Hb Zoetermeer *</p> <p>Hb M-Milwaukee-I *, Hb Melusine *, Hb Pitie-Salpetriere *, Hb Syracuse *, Hb Hounslow, Hb Fort Dodge, Hb Old Dominion (OD/BuT), Hb Camperdown, Hb Duarte, Hb Jura (Bamako)</p>
Z10	<p>Hb A, Hb Presbyterian, Hb Roubaix (Poland), Hb Silver Springs *, Hb El Escorial *, Hb Dallas *, Hb Olympia *, Hb Phnom Penh *, Hb La Corona *, Hb Uzes *, Hb Bougardirey-Mail *, Hb Saint Nazaire *, Hb Alzette *, Hb Antibes-Juan-Les-Pins *, Hb Arta (main peak) *, Hb Austin *, Hb Aztec *, Hb Beirut *, Hb Bethesda *, Hb Boghé *, Hb Bonn *, Hb Brem-sur-Mer *, Hb Brest *, Hb Brigham *, Hb Brisbane (Great Lakes) *, Hb Brugg *, Hb Buenos Aires (Bryn Mawr, major peak) *, Hb Buffalo (Reeuwijk) *, Hb Bushwick *, Hb Chicago *, Hb City of Hope *, Hb Coimbra (Ingelheim) *, Hb Columbia Missouri *, Hb Conakry *, Hb Djelfa (peak 1) *, Hb Fontainebleau *, Hb Frankfurt *, Hb Fukuoka *, Hb Godavari *, Hb Gorwihl (Hinchingsbrooke) *, Hb Gouda *, Hb Grange Blanche *, Hb Groene Hart (Bernalda) *, Hb Hamilton *, Hb Heathrow *, Hb Hekinan *, Hb Iraq-Halabja *, Hb Kosovo *, Hb La Desirade *, Hb Le Lamentin *, Hb Le Lamentin 2 *, Hb Linköping (Meilahti) *, Hb Lisbon *, Hb Little Rock *, Hb Lulu Island *, Hb Lyon-Bron *, Hb M-Boston (M-Osaka) *, Hb M-Saskatoon (main peak) *, Hb McKees Rocks *, Hb Malmö *, Hb Marseille (Long Island) *, Hb Milledgeville *, Hb Minneapolis Laos *, Hb Mizuho *, Hb Mosella *, Hb Noko *, Hb Okayama *, Hb Owari *, Hb Ozieri *, Hb Perth (Abraham Lincoln) *, Hb Potomac *, Hb Puttelange *, Hb Raleigh *, Hb Ravenscourt Park *, Hb Regina *, Hb Rhode Island (Southwark) *, Hb Riccarton *, Hb Rouen (Ethiopia) *, Hb Saclay *, Hb St Joseph's *, Hb San Diego *, Hb Santa Juana (Serres) *, Hb Savannah *, Hb Sydney *, Hb Taybe *, Hb Templeuve *, Hb Toulon *, Hb Twin Peaks *, Hb Ty Gard *, Hb Valletta *, Hb Verona *, Hb Villejuif *, Hb Villeparisis *, Hb Volga (Drenthe) *, Hb Westmead *, Hb Wood *, Hb Yaounde (Mataro) *, Hb Zoetermeer *</p> <p>Hb M-Milwaukee-I *, Hb Melusine *, Hb Pitie-Salpetriere *, Hb Syracuse *, Hb Hounslow, Hb Fort Dodge, Hb Old Dominion (OD/BuT), Hb Camperdown, Hb Duarte, Hb Jura (Bamako)</p>
Z11	<p>Hb Créteil, Hb Nouakchott, Hb Wayne (pic 1), Hb M-Iwate (M-Kankakee), Hb Camden (Tokuchi), Hb Hope</p> <p><i>Hb Créteil, Hb Nouakchott, Hb Wayne (peak 1), Hb M-Iwate (M-Kankakee), Hb Camden (Tokuchi), Hb Hope</i></p> <p>Hb A dégradée, Hb Vaasa, Hb Tacoma, Hb Providence (pic X-Asn), Hb Shepherds Bush, Hb Cook, Hb Corsica, Hb Pisa, Hb K-Woolwich, Hb Lombard, Hb J-Guantanamo, Hb Andrew Minneapolis, Hb J-Cape Town (alpha 1), Hb Kaohsiung (New York), Hb Fannin-Lubbock I, Hb Saint Claude, Hb Thionville, Hb Jackson (alpha 2), Hb J-Cape Town (alpha 2), Hb Strasbourg, Hb Osler (Fort Gordon), Hb Pierre-Bénite, Hb J-Auckland, Hb Nancy, Hb Himeji, Hb Singapore, Hb Jackson (alpha 1), Hb Tatras, variant de Hb A2 "I (I-Texas)"</p> <p><i>Denatured Hb A, Hb Vaasa, Hb Tacoma, Hb Providence (X-Asn peak), Hb Shepherds Bush, Hb Cook, Hb Corsica, Hb Pisa, Hb K-Woolwich, Hb Lombard, Hb J-Guantanamo, Hb Andrew Minneapolis, Hb J-Cape Town (alpha 1), Hb Kaohsiung (New York), Hb Fannin-Lubbock I, Hb Saint Claude, Hb Thionville, Hb Jackson (alpha 2), Hb J-Cape Town (alpha 2), Hb Strasbourg, Hb Osler (Fort Gordon), Hb Pierre-Bénite, Hb J-Auckland, Hb Nancy, Hb Himeji, Hb Singapore, Hb Jackson (alpha 1), Hb Tatras, "I (I-Texas)" Hb A2 variant</i></p>
Z12	<p>Hb Bart, Hb Nikaia, Hb Cemenelum, Hb Tokoname, Hb J-Cubujuqui, Hb Wayne (pic 2), Hb Hopkins-II (alpha 1), Hb J-Calabria (J-Bar), Hb J-Camagüey, Hb J-Tongariki, Hb J-Meerut (J-Birmingham - alpha 1), Hb Hopkins-II (alpha 2), Hb Zaïre, Hb J-Meerut (J-Birmingham - alpha 2), Hb Trollhättan, Hb Pyrgos (Mizunami), Hb Providence (pic X-Asp), Hb Suresnes, Hb J-Broussais (Tagawa-I - alpha 2), Hb Grady (Dakar - alpha 2), Hb Grady (Dakar - alpha 1), Hb Hikari, Hb J-Rajappen, Hb J-Anatolia, Hb J-Broussais (Tagawa-I - alpha 1), Hb J-Chicago, Hb J-Sardegna, Hb J-Cordoba, Hb J-Toronto, Hb J-Oxford (I-Interlaken), Hb J-Meinung (J-Bangkok), Hb Ube-2, Hb Hofu, Hb J-Cambridge (Rambam), Hb J-Abidjan, Hb Ulm, Hb J-Iran, Hb Riyadh (Karatsu), Hb Mexico (J-Paris-II - alpha 2), Hb Neuilly-sur-Marne, Hb Pontoise (J-Pontoise), Hb Ankara, Hb Mexico (J-Paris-II - alpha 1), Hb J-Paris-I (J-Aljezur - alpha 1), Hb Thailand, Hb J-Habana, Hb J-Baltimore (N-New Haven), Hb J-Wenchang-Wuming, Hb J-Paris-I (J-Aljezur - alpha 2), Hb K-Ibadan</p> <p><i>Hb Bart, Hb Nikaia, Hb Cemenelum, Hb Tokoname, Hb J-Cubujuqui, Hb Wayne (peak 2), Hb Hopkins-II (alpha 1), Hb J-Calabria (J-Bar), Hb J-Camagüey, Hb J-Tongariki, Hb J-Meerut (J-Birmingham - alpha 1), Hb Hopkins-II (alpha 2), Hb Zaïre, Hb J-Meerut (J-Birmingham - alpha 2), Hb Trollhättan, Hb Pyrgos (Mizunami), Hb Providence (X-Asp peak), Hb Suresnes, Hb J-Broussais (Tagawa-I - alpha 2), Hb Grady (Dakar - alpha 2), Hb Grady (Dakar - alpha 1), Hb Hikari, Hb J-Rajappen, Hb J-Anatolia, Hb J-Broussais (Tagawa-I - alpha 1), Hb J-Chicago, Hb J-Sardegna, Hb J-Cordoba, Hb J-Toronto, Hb J-Oxford (I-Interlaken), Hb J-Meinung (J-Bangkok), Hb Ube-2, Hb Hofu, Hb J-Cambridge (Rambam), Hb J-Abidjan, Hb Ulm, Hb J-Iran, Hb Riyadh (Karatsu), Hb Mexico (J-Paris-II - alpha 2), Hb Neuilly-sur-Marne, Hb Pontoise (J-Pontoise), Hb Ankara, Hb Mexico (J-Paris-II - alpha 1), Hb J-Paris-I (J-Aljezur - alpha 1), Hb J-Paris-I (J-Aljezur - alpha 1), Hb Thailand, Hb J-Habana, Hb J-Baltimore (N-New Haven), Hb J-Wenchang-Wuming, Hb J-Paris-I (J-Aljezur - alpha 2), Hb K-Ibadan</i></p>

TABLEAU / TABLE

CAPILLARYS HEMOGLOBIN(E) : VARIANTS POTENTIELS PRÉSENTS DANS CHAQUE ZONE
POTENTIAL VARIANTS LOCATED IN EACH ZONE

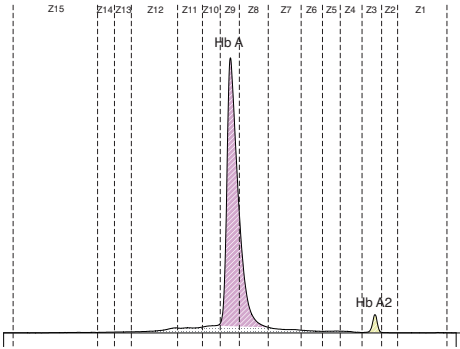
Zone	Hémoglobines / Hemoglobins (Hb)
Z13	Hb J-Europa, Hb N-Baltimore (Hopkins-I), Hb J-Rovigo, Hb Arta (pic mineur), Hb J-Norfolk (Kagoshima), Hb J-Kaohsiung (J-Honolulu)
	<i>Hb J-Europa, Hb N-Baltimore (Hopkins-I), Hb J-Rovigo, Hb Arta (minor peak), Hb J-Norfolk (Kagoshima), Hb J-Kaohsiung (J-Honolulu)</i>
Z14	Hb N-Seattle
	<i>Hb N-Seattle</i>
Z15	Hb H, Hb I-Toulouse, Hb Sudbury, Hb Kurosaki (alpha 1), Poly A (A->G): AATAAA->AATAAG of the alpha2 gene alpha-Thal-2, Hb Kurosaki (alpha 2), Hb F-Emirates, Hb N-Timone, Hb I (I-Texas, I-Philadelphia), Hb Shaare Zedek
	<i>Hb H, Hb I-Toulouse, Hb Sudbury, Hb Kurosaki (alpha 1), Poly A (A->G): AATAAA->AATAAG of the alpha2 gene alpha-Thal-2, Hb Kurosaki (alpha 2), Hb F-Emirates, Hb N-Timone, Hb I (I-Texas, I-Philadelphia), Hb Shaare Zedek</i>

* Pic non visible / Hidden peak

SCHÉMAS / FIGURES

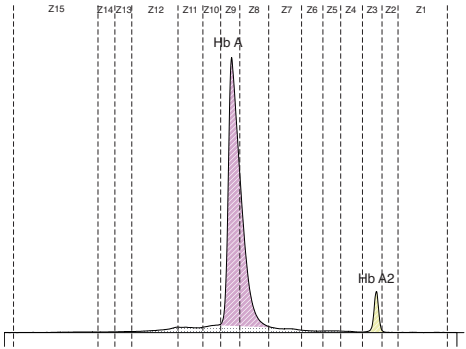
CAPILLARYS HEMOGLOBIN(E)
 PROFILS ÉLECTROPHORÉTIQUES - ELECTROPHORETIC PATTERNS

Figure 1



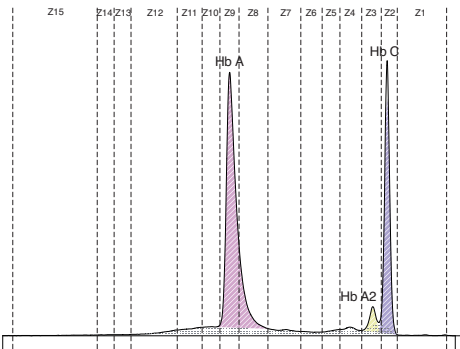
Sang normal
 Normal blood sample

Figure 2



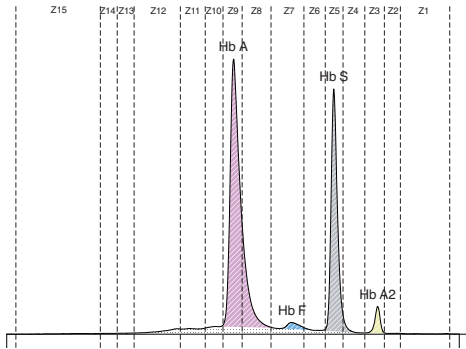
Sang bêta-thalassémique
 Blood sample with beta-thalassemia

Figure 3



Sang avec variant Hb C
 Blood sample with Hb C variant

Figure 4

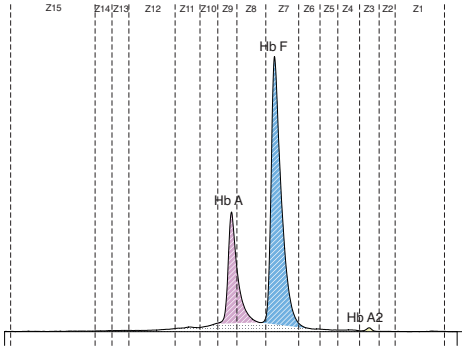


Sang avec variant hétérozygote Hb S
 Blood sample with Hb S heterozygote variant

SCHÉMAS / FIGURES

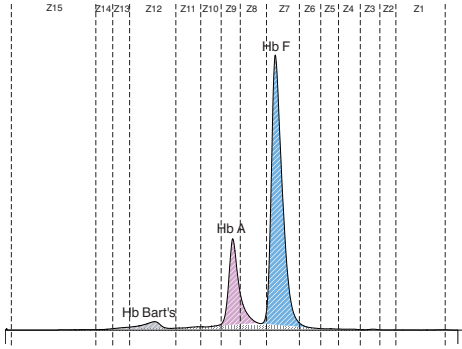
CAPILLARYS HEMOGLOBIN(E)
 PROFILS ÉLECTROPHORÉTIQUES - ELECTROPHORETIC PATTERNS

Figure 5



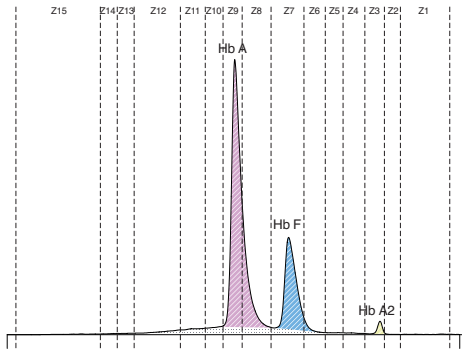
Sang de bébé (agé de 3 semaines)
Baby blood sample (3 weeks old)

Figure 6



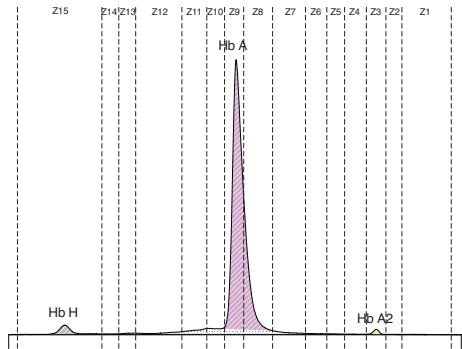
Sang de bébé avec Hb Bart's
Baby blood sample with Hb Bart's

Figure 7



Sang avec Hb F (jeune enfant)
Blood sample with Hb F (young child)

Figure 8

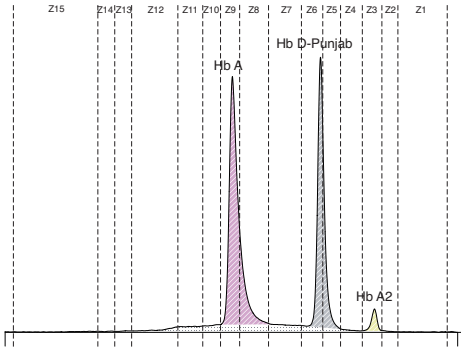


Sang avec Hb H
Blood sample with Hb H

SCHÉMAS / FIGURES

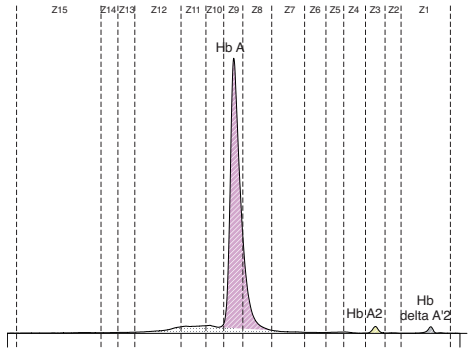
CAPILLARYS HEMOGLOBIN(E)
 PROFILS ÉLECTROPHORÉTIQUES - ELECTROPHORETIC PATTERNS

Figure 9



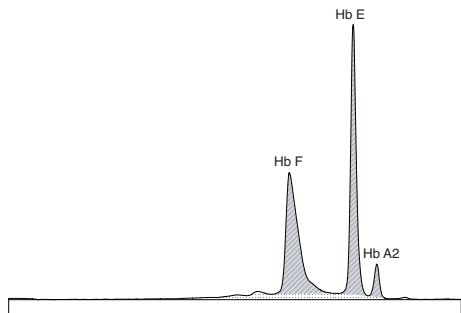
Sang avec variant Hb D-Punjab
 Blood sample with Hb D-Punjab variant

Figure 10



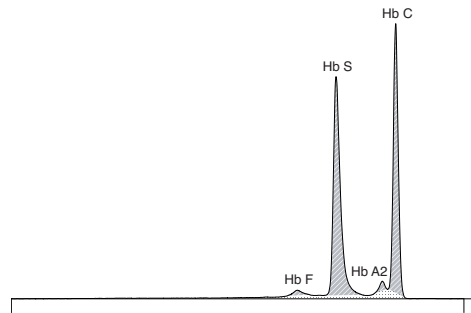
Sang avec variant delta Hb A'2
 Blood sample with delta Hb A'2 variant

Figure 11



Sang avec variant homozygote Hb E et fraction Hb F élevée
 Blood sample with homozygote Hb E variant and elevated Hb F

Figure 12

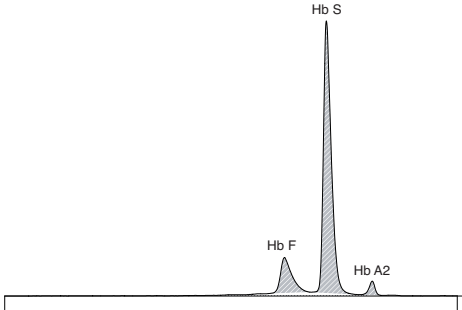


Sang avec variants hétérozygotes Hb S et Hb C
 Blood sample with Hb S & Hb C heterozygote variants

SCHÉMAS / FIGURES

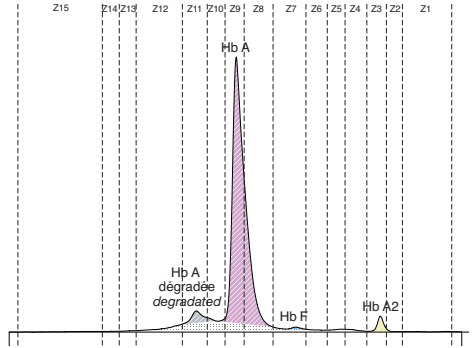
CAPILLARYS HEMOGLOBIN(E)
 PROFILS ÉLECTROPHORÉTIQUES - ELECTROPHORETIC PATTERNS

Figure 13



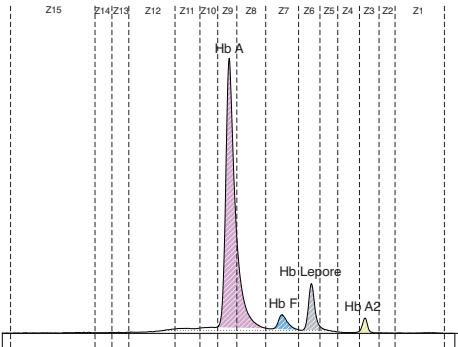
Sang avec variant homozygote Hb S (et Hb F)
 Blood sample with Hb S homozygote variant (and Hb F)

Figure 14



Sang avec Hb A dégradée (Hb A3) et Hb F faible
 Blood sample with degraded Hb A (Hb A3) and faint Hb F

Figure 15



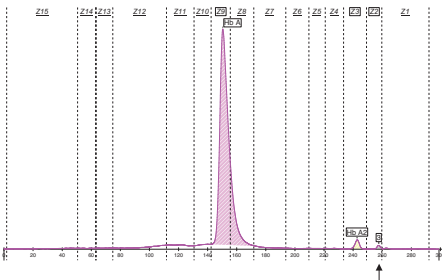
Sang avec variant Hb Lepore
 Blood sample with Hb Lepore variant

SCHÉMAS / FIGURES

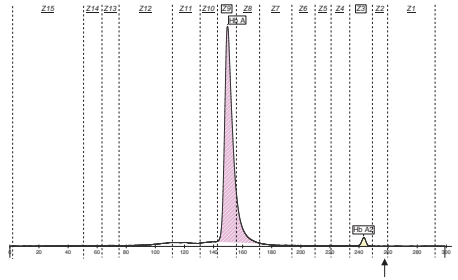
CAPILLARYS HEMOGLOBIN(E) - CAPILLARYS 2 FLEX-PIERCING
 PROFILS ÉLECTROPHORÉTIQUES - ELECTROPHORETIC PATTERNS

Figure 16

Fraction supplémentaire en zone de migration Z2 (protéines plasmatiques)
 Additional fraction in Z2 migration zone (plasmatic proteins)



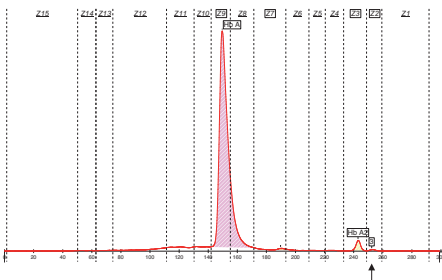
Analyse du sang total
 Whole blood analysis



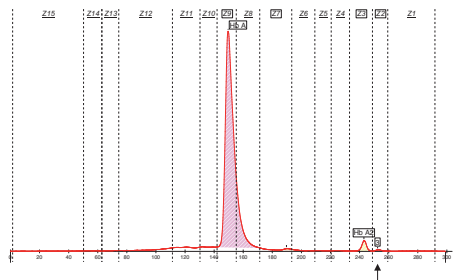
Analyse des globules rouges correspondants
 Analysis of corresponding red blood cells

Figure 17

Fraction supplémentaire en zone de migration Z2 (Hb Constant spring)
 Additional fraction in Z2 migration zone (Hb Constant spring)



Analyse du sang total
 Whole blood analysis



Analyse des globules rouges correspondants
 Analysis of corresponding red blood cells

Hb Constant Spring

SCHÉMAS / FIGURES

CAPILLARYS HEMOGLOBIN(E) - CAPILLARYS 2 FLEX-PIERCING
PROFILS ÉLECTROPHORÉTIQUES - ELECTROPHORETIC PATTERNS

Figure 18

Fraction supplémentaire en zone de migration Z15
Additional fraction in Z15 migration zone

