

## INSTRUCTIONS FOR DOCTORS

This Kit is intended for use in collection and preservation of samples until they arrive at the Igenomix facilities. These instructions are intended for medical workers. The Kit will transport endometrial samples. The materials included in this Kit can only be used by medical professionals, always in medical settings. This is not a self-assessment Kit. This Kit is not automated.

### Step 1: Contact us

Call: Landline: +966 549109444

or send us an email on [supportme@vitrolifegroup.com](mailto:supportme@vitrolifegroup.com)

- If you require more information about the ERA - EMMA - ALICE test, or
- If you need to arrange a test, or if you have any queries regarding the test service or test report.
- If this is the first time your doctor is requesting an ERA, EMMA, or ALICE test, please contact us for assistance with this test service. The EndomeTRIO manual can be downloaded from the Igenomix website or requested by emailing [supportme@vitrolifegroup.com](mailto:supportme@vitrolifegroup.com).

### Step 2: Receipt of the Kit

Review the contents of the EndomeTRIO kit and ensure that it contains:

- X-Igenomix ERA tube containing 1.5mL transparent preservation solution(1) (CE) (The tube should be used at least one week before its expiry date). Only use the tube supplied with the Kit.
- Additional plastic container (safety container for the tube).
- Pipelle<sup>®</sup> For endometrial biopsy (CE<sub>0459</sub>) (do not use if it is close to expiry).
- Plastic bag for return shipping (Courier).
- Test request form and informed consent.
- Igenomix QR Labels.\*

(1): RNAlater<sup>®</sup>. Only for shipping samples. Do not swallow.

\* **Stick a patient identifier label on the tube and another label on the Test Request Form, before sending to Igenomix.**

For further information, check the manufacturer's instructions: Pipelle<sup>®</sup> For endometrial biopsy, Ref. 1103000, Laboratoire CCD

**Note:** If the Igenomix ERA tube and/or Pipelle<sup>®</sup> expiry date has elapsed or the package is damaged, thus compromising the sterility of the material, dispose of it in accordance with current local regulations and contact Igenomix to receive a new Kit.

**The Kits must be stored at room temperature until they are used, never being submitted to temperatures above 35 °C. If the Kit has been stored for a long time, please check the expiry date of all materials before using.**

### Step 3: Sample collection

Warnings/Precautions: After carefully reading the EndomeTRIO manual, you must determine the type of cycle, medical procedure and biopsy date for the programmed embryo transfer.

#### Type of cycle and biopsy date:

- To perform the EMMA or ALICE tests (on their own or with the ERA test), the patient must not have taken any antibiotics at least 7 days before the biopsy or during the sampling procedure. If the patient has taken antibiotics in the previous month and during the biopsy procedure, it must be noted on the "Test Request Form".
- If only a EMMA or ALICE test is requested, the endometrial biopsy must be performed following the ERA procedure or between days 15 and 25 of the natural cycle (only for patients with regular cycles of 26-32 days). If the patient does not have regular cycles, we recommend performing an HRT cycle and taking the biopsy on P+5.
- If the patient requests the ERA test (on its own or with the other tests), the type of cycle for the biopsy must be the same as the chosen type of cycle for performing the programmed embryo transfer: HRT or natural cycle. The first biopsy must always be performed on P+5 in the case of an HRT cycle or on hCG+7/LH+7 in the event of a natural cycle, as ERA will assess the endometrium at the time of implantation:
  - HRT: either the routine procedure or our procedure may be used: the patient begins with estradiol from the 1st/2nd day of the menstrual cycle. An ultrasound assessment is performed 7-10 days prior. Begin with progesterone (P4) when the endometrium has a trilaminar appearance and thickness >6 mm with an endogenous P4 in serum <1 ng/mL (in the 24 hours prior to starting with exogenous P4). The day of the first dose of P4 is considered day P+0, and the biopsy is performed on P+5 (120 hours after the first dose of P4). (if higher, it would be recommended to cancel the biopsy).
  - Natural cycle: can be done either by determining the day of the LH peak or by using hCG to trigger ovulation (see manual). The day of the LH peak/use of hCG is considered LH+0/hCG+0 and the biopsy should be taken 7 days later, at LH+7/hCG+7 (168h after the determination of the LH peak or use of hCG). It is recommended to confirm that the endogenous progesterone level at LH+0/hCG+0 is <1ng/mL (if higher, it would be recommended to cancel the biopsy).
- The endometrial biopsy must not be performed in a stimulated cycle in any of the 3 tests (ERA, EMMA and ALICE).

#### Biopsy procedure and shipping:

- A single endometrial biopsy is sufficient for performing the EndomeTRIO test (includes ERA, EMMA and ALICE).
- Sample size: The endometrial biopsy must be taken from the uterine fundus using a Pipelle<sup>®</sup> (supplied with the Kit) or a similar catheter. It is very important to take the correct quantity of tissue - around 70mg (a fragment of approximately 7mm in size). Ensure that the sample contains endometrial tissue and not just blood and/or mucosa. Do not exceed the white line marked on the tube. This helps to prevent the genetic material from degrading.
- The sample must be transferred immediately to the tube supplied. Then shake the tube vigorously for several seconds.
- **Be sure to stick the Igenomix QR label on the tube and another on the application form.** If your kit does not contain labels, label the tube with the patient's initials and date of birth.
- In case of double and third biopsy in the same patient, **always** label (even if the kit contains Igenomix QR labels) the biopsy date on each tube.
- Incorrectly labelled or unidentified samples may be rejected
- The tube containing the sample must be stored immediately in the fridge (4-8 °C) and kept there for at least 4 hours. Once this time has elapsed, the sample may be sent to Igenomix at room temperature.
- ERA: The samples can be stored in the fridge for up to 3 weeks, or may be frozen at -20 °C (after 4 hours at 4-8 °C) if they are not going to be sent to Igenomix once the sample has been taken.
- EMMA and ALICE: given that the microbiome may fluctuate over time, we recommend shipping as soon as possible after the biopsy. We do not recommend delaying shipping beyond a week.
- Place the tube inside the additional container and then in turn, place this inside the Igenomix Kit. Finally, place the Kit inside the plastic bag for return shipping.

## INSTRUCTIONS FOR DOCTORS

- The following cases may involve contacting the customer again to confirm that the customer wants to process the sample under certain conditions:
  - Samples not accompanied by relevant documentation (Request Form and Informed Consent).
  - The documentation (Request Form and Informed Consent) is incorrectly completed.
  - The mandatory fields, marked on the forms by an asterisk (\*), are left blank.
  - The signature of the patient or the requesting doctor is missing on the Request Form and Informed Consent.
  - A different tube has been used to the one supplied with the Igenomix Kit for transferring the sample.
- This kit should only be used for the transport of samples.



### Step 4: Transporting the sample

- Samples can be sent at room temperature. Do not send frozen.
- We recommend using the cardboard packaging provided by Igenomix for returning the sample.
- Returns at room temperature must not exceed 5 days in transport time to ensure the preservative action of the solution in the tube.
- When the outdoor temperature is higher than 35 °C, additional measures must be taken to prevent deterioration of the sample during transport. We recommend using cold packs or similar devices, at all times ensuring that the sample does not become frozen.

If in doubt, please contact our customer service department.



### Step 5: Sample pick-up

To prevent the sample stability from being compromised, which could lead to a test failure or the need to take another sample, we recommend following these instructions:

#### Pick-ups in Saudi Arabia:

- Sample collection is available every day, Sunday through Thursday.
- To request a courier pick-up, please contact us at least 24 hours before your desired collection time.
- For scheduling and support, email Igenomix Customer Support & Logistics at: [supportme@vitrolifegroup.com](mailto:supportme@vitrolifegroup.com)

#### Pick-ups outside Saudi Arabia:

- Contact us to arrange courier pick-up based on your location.
- Submit your pick-up request at least 24 hours in advance.
- Before shipment, ensure your package includes all required documents: Airway Bill, Commercial Invoice, Non-Declaration shipping documents (These documents will be provided to you ahead of your scheduled collection.)

#### Additional Information:

- Please note that holidays may cause service disruptions. Igenomix will inform you promptly of any changes to pick-up schedules.
- We recommend sending samples as quickly as possible in order to ensure the quality of the sample.



### Step 6: Test results

Igenomix will send the test results within **15 Business days** after our laboratory receives the sample.

The ERA test result includes a recommendation for performing a personalized embryo transfer. The EMMA and ALICE report includes suggested treatment where necessary.

In some cases, a new biopsy may be requested (for ERA, EMMA, ALICE or EndomeTRIO). In this case, we will provide details on how to proceed.

For clinical consultations associated to the tests: [era@igenomix.com](mailto:era@igenomix.com) - [emma.alice@igenomix.com](mailto:emma.alice@igenomix.com)