OFFICE USE ONLY
Received date:

EndomeTRIO Test Requisition Form (ERA/EMMA/ALICE)

All shaded fields must be completed. If required fields are not completed, results may be delayed.
Prior to collecting the sample, please read the Manual that you can find on the Igenomix website: section Reproductive Health / Specialists

REQUESTED ANALYSIS

☐ ERA	☐ EMMA (includes ALICE)	☐ ALICE	☐ EndomeTRIO
Endometrial Receptivity Analysis	Endometrial Microbiome Metagenomic Analysis	Analysis of Infectious Chronic Endometritis	ERA + EMMA + ALICE

CLINIC INFORMATION

CLINIC NAME:		
ADDRESS:		**TELEPHONE:**
CITY:	**COUNTY / PROVINCE:**	**POSTCODE:**
DOCTOR REQUESTING TEST:		
E-MAIL ADDRESS TO RECEIVE RESULTS:		

PATIENT INFORMATION

NAME AND SURNAMES/INITIALS/IDENTIFICATION CODE:			
D.O.B.: _____ /_____ /_____ DD MM YYYY		**MRN/Unique patient ID:**	**ETHNICITY:**
WEIGHT (kg):	**HEIGHT (cm):**	**REPORT LANGUAGE:** ☐ SPANISH ☐ ENGLISH ☐ ITALIAN ☐ PORTUGUESE	

CLINICAL INDICATION OF TEST

☐ **Endometrial analysis** ☐ **Chronic Endometritis** ☐ **Previous STIs** ☐ **Hydrosalpinx** ☐ **Endometriosis**
☐ **Recurrent miscarriage** ☐ **Implantation failure - No. of implantation failure (failed attempts):** _____

Summarised medical history or relevant background:

SIGNATURES

DOCTOR AUTHORISATION	PATIENT CONSENT
I certify that the information on this requisition form is correct to the best of my knowledge and that I have requested the above test based on my professional judgement of clinical indication. I have explained the limitations of this test and I have answered any question with my medical judgement. I understand that Igenomix (Part of Vitrolife Group) may need additional information and I agree to provide this information if necessary.	By signing this requisition form, I voluntarily request Igenomix (Part of Vitrolife Group) to carry out the test indicated above. I have read and received a copy of the informed consent, included in the following pages. The risks, benefits and limitations of this test have been explained to me.
DOCTOR'S SIGNATURE: _____	**PATIENT'S SIGNATURE:** _____
DATE: _____ /_____ /_____ DD MM YYYY	**DATE:** _____ /_____ /_____ DD MM YYYY
DOCTOR PERFORMING BIOPSY:	**SIGNATURE OF DOCTOR PERFORMING BIOPSY:**

NAME AND SURNAMES/INITIALS/IDENTIFICATION CODE:

CYCLE DATA

Select and fill only one cycle type.
All shaded fields must be filled for your selected cycle type.
It is not recommended to perform these tests in Controlled Ovarian Stimulated cycles.

TYPE OF CYCLES VALID FOR ERA / EMMA&ALICE /ENDOMETRIO TESTS

1 **HORMONE REPLACEMENT THERAPY:**
(Cycle without ovulation)
☐ HRT (estradiol + progesterone)

DATE AND TIME OF 1ST PROGESTERONE DOSE (Day P+0):
Date: _____/_____/_____ (DD/MM/YYYY) Hour: _____:_____ (hh:min) (00:01 to 23:59)

OR

2 **NATURAL CYCLE:**
(Cycle with ovulation)
☐ hCG TRIGGER ☐ LH SURGE

DATE AND TIME OF hCG TRIGGER OR LH SURGE (Day hCG+0 / Day LH+0):
Date: _____/_____/_____ (DD/MM/YYYY) Hour: _____:_____ (hh:min) (00:01 to 23:59)

OR

3 **MODIFIED NATURAL CYCLE:**
(Cycle with ovulation supplemented with P_4):
☐ hCG TRIGGER + P_4
☐ LH SURGE + P_4
P_4=Progesterone

DATE AND TIME OF hCG TRIGGER OR LH SURGE:
Date: _____/_____/_____ (DD/MM/YYYY)
Hour: _____:_____ (hh:min) (00:01 to 23:59)

DATE AND TIME OF 1ST PROGESTERONE DOSE:
Date: _____/_____/_____ (DD/MM/YYYY)
Hour: _____:_____ (hh:min) (00:01 to 23:59)

ENDOGENOUS PROGESTERONE MEASUREMENT AT LH+0/hCG+0 (natural cycles) OR WITHIN 24h PRIOR STARTING EXOGENOUS P_4 (HRT cycle)

ENDOGENOUS PROGESTERONE VALUE (must be <1ng/ml at LH+0/hCG+0/P+0): _____ (ng/ml) Date of measurement: _____/_____/_____ (DD/MM/YYYY)

DAILY DOSE OF EXOGENOUS PROGESTERONE: _____ PROGESTERONE ADMINISTRATION: ☐ VAGINAL ☐ INTRAMUSCULAR ☐ ORAL

ENDOMETRIAL THICKNESS: _____mm THICKNESS MEASUREMENT DATE: _____/_____/_____ (DD/MM/YYYY)

ADDITIONAL MEDICATION USED: ☐ NO ☐ YES – PLEASE INDICATE: _____

TYPE OF CYCLES VALID FOR EMMA AND ALICE TESTS ONLY (not for ERA / EndomeTRIO test)

☐ **NATURAL CYCLE BETWEEN DAYS 15 TO 25** (only for patients with regular cycles of 26-32 days). **Day of cycle:** _____ **LMP:** _____/_____/_____ (DD/MM/YYYY)

OR

☐ **ORAL CONTRACEPTIVE PILLS** (between days 14-21 of active pills -*if placebo pills given*- or day 14 onwards of active pills - *if not placebo pills given*)
OCP BRAND: _____ **Day of cycle on the biopsy day:** _____ **Type of intake:** ☐ ACTIVE PILLS CONTINUOUSLY ☐ WITH PLACEBO/BREAK

AMENORRHEAL PATIENT? ☐ NO ☐ YES

SAMPLE INFORMATION

BIOPSY METHOD:
☐ Pipelle ☐ Hysteroscopy ☐ Other method:_____

BIOPSY DATE AND TIME Date: ____/_____/_____ (DD/MM/YYYY) Hour: _____:____ (hh:mm) (00:01 to 23:59)

Has the patient had ERA/EMMA/ALICE previously? ☐ No ☐ Yes

ERA biopsy No.* _____ EMMA biopsy No. _____ ALICE biopsy No. _____
*If repeat biopsy, were ERA mock cycle protocols replicated (i.e. same medications, dose, etc.)? ☐ No ☐ Yes

ANTIBIOTICS RELATED INFORMATION (If performing EndomeTRIO or EMMA/ALICE)

PREVIOUS ANTIBIOTICS USE: ☐ NO ☐ YES - (Ingredient): _____

Dose: _____ Start date: _____/_____/_____ (DD/MM/YYYY) Last date: _____/_____/_____ (DD/MM/YYYY)

First biopsy: Antibiotics taken within the month prior to the sample collection. **Re-biopsy:** Antibiotics taken between previous sample and current one

ANTIBIOTICS ALLERGIES: ☐ No
☐ Yes - SPECIFY: ☐ β-lactam ☐ Macrolids ☐ Tetracyclines ☐ Lincosamides ☐ Nitroimidazoles ☐ Trimethoprim/Sulfonamides

If you need more space to fill any of the fields, you could use the field "Summarised medical history" in the section "Clinical Indication of the Test"

Informed consent for endometrial biopsy and evaluation

DESCRIPTION, PURPOSE AND ADVANTAGES OF PERFORMING THE ANALYSIS

The Endometrial Receptivity Analysis (ERA) is a molecular diagnostic method that determines if the endometrium (the mucous lining inside the womb) is receptive after five full days of progesterone exposure, when the endometrium is prepared for embryo implantation. The test is based on simultaneously measuring, using Next Generation Sequencing (NGS), the expression profile of 248 genes of endometrial cells that have been previously identified as the transcriptomic signature of endometrial receptivity and a bioinformatics tool (predictor) that gives a diagnosis with a specific diagnostic probability.

Consequently, ERA helps determine if the endometrium is in optimal conditions for embryo implantation, allowing the embryo transfer to happen when it is ready, thereby increasing the chances of success of in-vitro fertilisation (IVF).

The Endometrial Microbiome Metagenomic Analysis (EMMA) is a molecular test that provides microbiota information in endometrial tissue by analysing a customized panel including information about Lactobacillus and potentially pathogenic bacteria of the reproductive tract, some of them related to Chronic Endometritis (CE). This method is based on detecting bacterial DNA through Real-Time PCR, which translates into different profiles that have been linked to the success of pregnancy. EMMA test can be performed on an endometrial biopsy taken following the same protocol as ERA test or between days 15 and 25 of the natural cycle (only for patients with regular cycles between 26-32 days). If the patient does not cycle regularly, we recommend performing an HRT cycle and taking the biopsy during the progesterone exposition days (preferably P+5). The biopsy can be also collected using combined Oral Contraceptive Pills (OCPs) between days 14-21 of active pills (if the patient takes placebo pills) or from day 14 and onwards if takes active pills continuously (note: not all OCPs are valid for EMMA testing, it's recommended to consult with Igenomix about its validity before scheduling the biopsy). EMMA test can be beneficial for any woman who wishes to achieve pregnancy, especially those with recurrent implantation failure and recurrent pregnancy loss, by analysing the microbial environment of the uterine cavity including bacterial pathogens most often identified as causing Chronic Endometritis (CE). The EMMA test results report provides an interpretation of the data obtained and a recommendation, to achieve an optimal endometrial microbiota, which as described in the scientific literature, increases the chances of getting a pregnancy. The EMMA test always includes the ALICE test.

Analysis of Infectious Chronic Endometritis (ALICE) is a molecular test performed using Real-Time PCR, which detects the presence of DNA from potentially pathogenic bacteria that most frequently cause chronic inflammation of the endometrium, known as Chronic Endometritis (CE). This disease has been linked to infertility and obstetric complications. Like the EMMA test, ALICE can be performed on an endometrial biopsy taken following the same protocol as ERA test or between days 15 and 25 of the natural cycle (only for patients with regular cycles between 26-32 days). If the patient does not cycle regularly, we recommend performing an HRT cycle and taking the biopsy during the progesterone exposition days (preferably P+5). The biopsy can be also collected using combined Oral Contraceptive Pills (OCPs) between days 14-21 of active pills (if the patient takes placebo pills) or from day 14 and onwards if takes active pills continuously (note: not all OCPs are valid for EMMA testing, it's recommended to consult with Igenomix about its validity before scheduling the biopsy). ALICE test can be helpful in determining which pathogenic bacteria are present in the endometrium and probably causing chronic inflammation of the uterine cavity. These results may help determine the most appropriate antibiotics to eliminate the pathogens causing the disease.

PROCEDURE, RISKS AND LIMITATIONS

These analyses require a biopsy from the endometrium, performed by inserting a very fine cannula through the vagina into the uterus, from which a small piece of endometrial tissue is taken. This small endometrial biopsy is enough to carry out the three procedures (ERA, EMMA and ALICE) simultaneously. You may feel some discomfort from the procedure, and may bleed a little after the biopsy, but it is a common process with no added risk.

To process the sample, the test request and consent form will need to be correctly completed and signed. If this is not the case, the analysis may be put on hold until the information required has been given to the laboratory.

Given the complexity of the genetic tests and the significant implications of the test results, the results obtained must be interpreted in conjunction with other clinical data, within the general context of a medical practice run by healthcare professionals. The result reports are strictly confidential.

The results of the test will be available in a maximum of 15 business days. A small percentage of samples may be delayed due to unforeseeable causes. Should this occur, the corresponding clinic will be notified.

ERA: The biopsy must be taken seven days after the LH surge (natural cycle), seven days after the hCG administration (natural hCG cycle) or after five full days of progesterone exposure in a HRT cycle. If the ERA analysis detects a displaced window of implantation, the result will recommend the optimal day/time for embryo transfer other than the one performed for the biopsy. In some cases, a second endometrial biopsy may be necessary and will be taken following the test result. In approximately 1% of cases, a non-informative diagnosis is obtained. In these cases, a new endometrial biopsy will be required. There is a small chance (less than 5%) that a sufficient quantity and/or quality of sample will not be obtained to make a diagnosis. In these cases, a new endometrial biopsy will be required.

EMMA/ALICE: The biopsy should be taken as close to the embryo transfer cycle as possible, since the microbiota could fluctuate in time and in response to different factors (hormonal changes, hygiene habits, fluctuations in general health, sexual relations, etc.). It is also important that the patient has not taken antibiotics within 7 days of taking the biopsy, and if it cannot be avoided, it should be clearly indicated on the test application form. A result may not be possible in some cases. This could happen because there is not enough genetic material to analyse or because the sample has become contaminated at some point in the process. If this occurs, the request for a new sample will be valued.

Informed consent for endometrial biopsy and evaluation

DATA PRIVACY, STORAGE AND SAMPLES USED FOR RESEARCH

Your privacy is a priority for the Igenomix Group. Your identity and all data referring to your personal information will be confidential and only Igenomix personnel will be permitted access to this information, along with the relevant authorities when required by the laws of the applicable jurisdiction.

Below are listed the different purposes for which your personal data will be processed either by the Clinic or the healthcare provider, or by Igenomix:

Processing of your personal data for the purpose of carrying out the genetic test.

For this purpose, Igenomix UK ("Igenomix") is processing your personal data exclusively on behalf of your clinician/healthcare provider. Your clinician/healthcare provider is the data controller and Igenomix is the data processor. This entails that for this purpose, Igenomix will only process your personal data following the instructions and directions of your clinician/health care provider.

Hence, the purpose and means for the processing of your personal data to carry out the test is mainly determined by your clinician/healthcare provider, who will have provided you with all relevant privacy information regarding the processing of your personal data in line with the applicable regulations.

Therefore, if you have any queries regarding the processing of your personal data for this purpose, you may contact the data controller (your clinician/ healthcare provider) at the address it has provided you in its own privacy policy. If you need to contact Igenomix, you can reach out to our Data Protection Officer through the following e-mail address privacy@igenomix.com or with postal mail to the address Igenomix UK, Surrey Technology Centre, 40 Occam Road, Guildford GU2 7YG.

The sample will be analysed by Igenomix or an associated group selected by Igenomix on an international level. Igenomix reserves the right to carry out part or all of the analyses included in the test through third party laboratories certified with recognised international quality standards, and with the same level of data protection security measures. Any results obtained in this way will be inspected by Igenomix and this circumstance will be indicated in the final report issued.

Use of Anonymised Information for Continuous Improvement, Internal Training and Knowledge Development

In accordance with applicable international standards (ISO, CAP, CLIA or others), and applicable legislation, we must perform validations, quality controls and internal audits to ensure the accuracy, security and reliability of our results. These activities are an essential part of Igenomix service. The test results generated in Igenomix marketed service may be used in a completely anonymised way (without the possibility of linking them to your identity) for: (1) Continuous Improvement; Optimise protocols, techniques and tools, ensuring increasingly effective and safe care. (2) Team Training; Train our staff, maintaining a high level of experience and knowledge. (3) Internal Knowledge Development; To deepen the understanding of genetic and reproductive processes, promoting improvements and innovations that benefit the community at large. These activities will in no way affect the confidentiality and integrity of your personal information, as the individual from whom the data originates cannot be identified or traced back.

Sample storage

Samples collected as part of Igenomix marketed services will be stored temporarily in accordance with applicable laws and standards, including ISO 15189, which ensures quality and integrity. The sample will be kept under controlled conditions (e.g., proper temperature and security) to maintain its suitability for testing.

The sample will be retained only for as long as necessary for the intended purpose, after which it will be securely destroyed or anonymized in a manner that protects your privacy.

Exceptions to this process shall only be made where longer retention is legally required or explicitly authorized by the individual, with their informed consent.

HAVING READ AND UNDERSTOOD THE FOREGOING, I AM AWARE OF:

The indications, procedure, success rate, risks and complications of the proposed treatment, as well as the financial cost of said test(s).

The fact that medical staff are at my disposal to expand on any aspect of the information that is not sufficiently clear to me.

I have understood the explanations given to me in clear and simple language, and the clinician who saw me allowed me to make comments, clarifying any issues I raised and informing me that I may freely withdraw my consent at any time.

I am satisfied with the information received and I freely submit to undergoing an endometrial biopsy at the assisted reproduction Centre/Clinic which I have attended. I also consent to the endometrial tissue sample being sent to Igenomix (Part of Vitrolife Group) facilities for the purpose of carrying out the aforementioned test(s).

I also accept that the results of the test(s) may be passed on to my clinician, so that he or she can advise me correspondingly on the suitable IVF treatment.