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 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

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 evaluates the overall profile of bacteria present in the endometrium. This method is based on detecting bacterial DNA through NGS sequencing. As described in the scientific literature, a bacterial profile free of pathogens and *Lactobacillus*-dominated, is related to a higher probability of achieving a successful pregnancy. This test is performed with an endometrial biopsy after five days of progesterone exposure or between days 15-25 of the natural cycle. EMMA can be beneficial for any woman who wishes to be a mother, especially those with recurrent implantation failure, by analysing the bacterial DNA profile of the uterine cavity, including bacterial pathogens most often identified as causing Chronic Endometritis (CE). The EMMA results report provides an interpretation of the data obtained and a recommendation, in order to obtain a *Lactobacillus*-dominated reproductive tract, which as described in the scientific literature, increases the chances of achieving a pregnancy. The EMMA test includes the ALICE test.

Analysis of Infectious Chronic Endometritis (ALICE) is a molecular test, performed by massive sequencing (NGS), which detects the presence of DNA from pathogenic bacteria that most often cause chronic inflammation of the endometrium, known as Chronic Endometritis (CE). This disease has been associated with infertility and obstetric complications. As for the EMMA test, endometrial biopsy may be taken after five days of progesterone exposure or between days 15-25 of the natural cycle. ALICE can be beneficial for identifying and quantifying DNA from pathogenic bacteria that are found in the uterine cavity and that could cause chronic inflammation of the uterine cavity. These results can help the most appropriate choice of antibiotics to eliminate disease-causing pathogens.

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.

DATA PRIVACY, STORAGE AND SAMPLES USED FOR RESEARCH

We would like to inform you that your personal data will only be processed to: (1) Fulfil the obligations arising from the provision of the services contracted by you; (2) Check and guarantee the quality of the services provided (internal audits, quality controls, laboratory validation studies); (3) For educational purposes, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (4) For research purposes, scientific publications and presentations, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (5) Personally address any doubts or suggestions made by the patient during the process and monitor the proper performance and resolution of the test, including the indefinite retention of your data, except where local laws of the applicable jurisdiction state otherwise; and (6) Contact you in the future to request an evaluation of the services received, send commercial communications (including 'cross-selling' and 'upselling') from associated companies, and also to invite you to participate in market research and the development of new products.

You also authorise your clinician to send us the information regarding the personalised embryo transfer associated with the result of this test, in order to complete the clinical follow-up of the endometrial evaluation.

You also declare that you understand and accept that you will not obtain, either now or in the future, any economic benefit for any research carried out, and that there is no intention to compensate you for the products developed from any research.

The sample will be analysed by Igenomix (Part of Vitrolife Group) or an associated group selected by Igenomix on an international level. Igenomix (Part of Vitrolife Group) 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, or failing this, they will be periodically assessed by Igenomix (Part of Vitrolife Group). Any results obtained in this way will be inspected by Igenomix (Part of Vitrolife Group) and this circumstance will be indicated in the final report issued.

Samples and all associated data will be retained in the laboratory in accordance with the Igenomix's specimen retention policy which is in accordance with all the legal requirements.

Pursuant to the laws on the Protection of Personal Data, the requesting party must have the patient's consent to perform the diagnostic tests requested and to process their data. You may, at any time, exercise your rights regarding access, rectification, opposition, deletion, automated decisions, limitation, portability, by sending an email to privacy@igenomix.com, providing proof of the requesting party's identity.

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.