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Endometrial analysis request form

All fields marked with * are mandatory

***ANALYSIS REQUESTED** ☐ ERA ☐ EMMA ☐ ALICE ☐ EndomeTRIO

CLINICIAN INFORMATION

Date: _____

*Clinic: _____ *Doctor: _____

Address: _____

City: _____ Province: _____ Postcode: _____

Telephone: _____ Email: _____

PATIENT INFORMATION

*Name and surnames/initials/identification code: _____

*Date of birth: _____ MRN/Unique patient ID: _____ *Ethnicity[1]: _____

Weight: _____kg Height: _____cm Results report language: ☐ Spanish ☐ English ☐ Italian ☐ Portuguese

1- This field is only required if you have selected the ALICE or EMMA tests.

SAMPLE DETAILS

Type of sample: Endometrial biopsy. Biopsy method: ☐ Pipelle ☐ Hysteroscopy ☐ Other: _____

Type of cycle:

☐ **HRT: P+** _____ (e.g. P+5) *First day of progesterone[2]: _____ Time: _____ (00:01-23:59)AM/PM
Endogenous progesterone P+0:_____ ng/ml or _____ nMol/l Date measured: _____

☐ **Natural cycle**: **LH+** _____ (e.g. LH+7) – *Day of LH[2] surge: _____ Time: _____ (00:01-23:59) AM/PM

☐ **hCG+** ____ (e.g. hCG+7) – *Day of hCG[2] injection: _____ Time: _____ (00:01-23:59) AM/PM

☐ **Natural cycle between days 15 and 25** (for 26 to 32 day cycles), **only for EMMA/ALICE *Day of cycle:**_____

2- The first day with progesterone is considered P+0. The LH surge day is considered LH+0. The day of the hCG injection is considered hCG+0.

Biopsy details:

*Date of biopsy: _____ Time: _____ AM/PM

Endometrial thickness: _____mm Date: _____ Has an ERA/EMMA/ALICE test been performed before? NO ☐ YES ☐

* ERA Biopsy No. _____ *EMMA Biopsy No. _____ *ALICE Biopsy No. _____ ☐ Two biopsies in the same cycle[3]

3- The 2nd sample will be analysed if the result of the 1st is Non-Receptive with a recommendation to perform a new biopsy.

INDICATION OF TEST

☐ Endometrial analysis ☐ Implantation failure – Number of failed attempts: _____

☐ Chronic endometritis ☐ Endometriosis ☐ Recurrent miscarriage ☐ Hydrosalpinx ☐ Previous STIs[4]

Summary of clinical record or relevant medical history: _____

_____

*Has taken antibiotics in the last three months[5]: ☐ NO ☐ YES: *Active ingredient[5]: _____ *Dosage[5]:_____

*Duration of treatment[5]: _____ *Date on which it was administered[5]:_____

*Existing allergies to any antibiotic?[5] ☐ NO ☐ YES. Specify which[5]: ☐ β-lactams ☐ Macrolides ☐ Tetracyclines ☐ Lincosamides ☐ Nitroimidazoles ☐ Trimethoprim/ Sulfonamides

4- Sexually transmitted infections

5- This field is only required if you have selected the ALICE or EMMA tests.

Doctor authorisation

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 may need additional information and I agree to provide this information if necessary.

Doctor's signature_____ Date: _____/_____/_____

Patient consent

By signing this requisition form, I voluntarily request Igenomix 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.

Patient's signature_____ Date: _____/_____/_____

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, which translates into different profiles that have been linked to the success of pregnancy. This test can be performed on an endometrial biopsy after five days of exposure to progesterone in a hormone replacement therapy (HRT) or between days 15-25 of the natural cycle. EMMA can be beneficial for any prospective mother, especially those with recurrent implantation failure, by analysing the microbial environment of the uterine cavity including the pathogens that cause Chronic Endometritis (CE). EMMA will recommend appropriate actions to restore the healthy physiological microbial environment of the uterus for embryo implantation. EMMA includes ALICE.

Analysis of Infectious Chronic Endometritis (ALICE) is a molecular test, performed by NGS, which detects the presence of pathogenic bacteria that most frequently cause chronic inflammation of the endometrium, known as CE. This disease has been linked to infertility and obstetric complications. Like EMMA, ALICE can be performed on an endometrial biopsy after five days of exposure to progesterone in an HRT cycle or between days 15-25 of the natural cycle. ALICE can be helpful in determining which pathogenic bacteria are present in the uterine cavity and which may be the cause of 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 10 working 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 an 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, as endometrial bacteria may fluctuate over time and in response to different factors (hormonal changes, hygiene habits, general changes in health, sexual intercourse, etc.). It is important to make sure that the patient has not taken standard antibiotics in the three months prior to taking the biopsy. If this cannot be avoided, it should be indicated in the request form for endometrial evaluation. The result may not allow a diagnosis to be established in some cases, this may occur because there is not enough DNA in the sample, not enough bacterial DNA, or because the sample has become contaminated during collection or transport. If this happens, a new endometrial biopsy will be required.

DATA PRIVACY, STORAGE AND SAMPLES USED FOR RESEARCH

Your privacy is a priority for the Igenomix Group ("Igenomix"). 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. You will find further information on the Igenomix Privacy Policy, along with all your rights at www.igenomix.com, or this information may be provided to you upon request by sending an email to privacy@igenomix.com.

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 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, or failing this, they will be periodically assessed by Igenomix. Any results obtained in this way will be inspected by Igenomix and this circumstance will be indicated in the final report issued.

Pursuant to the laws on the Protection of Personal Data[1], 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 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.

[1] **For non-US patients:** customers residing outside the United States under certain jurisdictions may at any time request to have their personal information deleted from our active databases, subject to the applicable laws and regulations in each jurisdiction. Although we can delete your personal information from our active databases, part or all of your personal information shall remain stored in back-up files for the purpose of complying with legal, regulatory or other requirements. Information that has already been coded and/or anonymised may not be recoverable or traceable for destruction, deletion or modification. If you wish to have your personal information removed from our active databases, please contact us at privacy@igenomix.com.