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OPERATION MANUAL

BeREADY® test aims to provide physicians with the prognosis of endometrial receptivity based on the molecular biomarker profile of the analyzed biopsy. The test analysis the expression level of 68 receptivity biomarkers. The biomarker profiling is carried out by TAC-seq technology, Illumina Inc. NGS sequencing, and beREADY-2 data analysis software. Depending on the result of this analysis, the physician may use it to guide personalized treatment or embryo transfer. Following beREADY test recommendations do not guarantee embryo implantation. Failed implantation may also be caused by other factors such as various pathologies, poor embryo quality, and embryo genetic abnormalities.

The patient must receive the necessary information about the beREADY test from the physician. The patient has to sign the beREADY informed consent prior to the biopsy. The physician has to fill in the requisition form.

The beREADY test kit contains a coded biopsy transportation tube, informed consent, absorbing tube holder in mini grip plastic bag, security seal, leaflet, operation manual, and transportation box. Inside the box, there is a short operation manual. Outside the box, the prepaid courier label, lot number, and expiration date are marked. The doctor is responsible for checking the expiration date before use. An intact kit should be used if the transportation box or biopsy tube is damaged. Please discard the damaged item according to the best practice of recycling.

Endometrial biopsy collection procedure

Endometrial biopsies can be taken in an HRT or natural cycle. The endometrial biopsy is taken by Pipelle catheter or similar that is not included in the kit. Be sure that the biopsy contains endometrial tissue and not only blood and mucus. After the biopsy has been performed, transfer the biopsy to a prefilled and coded beREADY transportation tube. The tube contains a transportation solution.

IMPORTANT: release **1–2.5 cm** of endometrial biopsy into the transportation tube. Discard the rest of the biopsy or store it in the clinic in deep-frozen condition. Close the transportation tube tightly and invert the tube several times. Place the transportation tube into the **refrigerator (4 – 8˚C) for a minimum of four hours.**
After this time, ship the biopsy to beREADY laboratory at ambient temperature.

Biopsy collection in Hormone Replacement Therapy (HRT) cycle

The day of the biopsy in an HRT cycle is determined as follows: ultrasound assessment will be performed between 7–10 days of estradiol priming. Progesterone treatment will be started when an endometrium ≥6 mm is obtained and the progesterone level is <1 ng/ml. The day on which the progesterone treatment begins is referred to as P+0, and the biopsy is taken exactly on day P+5 or 120h. Be convinced that there is no ovulation before the first day of progesterone intake.

Biopsy collection in Natural Cycle

The day of the biopsy in a natural cycle is determined as follows. If the follicles are >17 mm, hCG is injected. The day of the initial hCG administration is considered as day hCG+0. The endometrial biopsy will be taken after seven days (hCG+7 or 168h). Similarly, without hCG administration, a biopsy can be taken after a seven-day after the ovulation test has turned positive (LH+7).

The standard procedure to order and send biopsy

To order beREADY test, go to the webpage orderbeready.ee and use your clinic unique beREADY ordering code (provided) to log in and fill in the form.

After sampling the biopsy, place the biopsy into the transportation tube and place it into **the refrigerator (4–8˚C) for four hours.** Send the biopsy at ambient temperature with the following instructions:

1) Place transportation tube into absorbing tube holder in mini grip plastic bag, seal the bag and place it in the transportation box.
2) Place signed informed consent form into the transportation box.
3) Order the courier by the following manual inside the box lid.
4) Close the transportation box and seal the lid with provided safety tape.

Coding

Informed consent and biopsy transportation tube have the same patient code.

Interpreting the beREADY test results

Test results are available for the physician who placed an order. Test results for download are available on the webpage orderbeready.ee with the clinic's unique beREADY ordering code.

Receptive: This biomarker analysis detected that the biopsy has a receptive profile.

Pre-receptive: This biomarker analysis revealed that the biopsy is not receptive yet. The endometrium needs an extra day or two to mature. It is recommended to adjust timing according to the beREADY report and take a re-biopsy.

Post-receptive: This biomarker analysis revealed that the biopsy is not receptive anymore. The endometrium is over matured, which has happened potentially a day or two ago. It is recommended to adjust timing according to the beREADY report and take a re-biopsy.

Non-informative result: The profile analyzed does not match the control biomarker profiles present in the beREADY test. It is recommended to repeat the biopsy sampling.

Insufficient RNA: The analysis procedure was not initiated due to the low nucleic acid (RNA) amount extracted from the biopsy. It is recommended to take a new biopsy.

Invalid RNA: It was not possible to determine the biomarkers profile due to the poor quality of RNA. It is recommended to take a new biopsy and follow the instructions carefully.