Know-how "Innovative genetic test for determining the causes of infertility "GENTERF""*

Description of the technology and proposed kit:

In vitro diagnostic medical device (*know-how*) consisting of the following documents:

1. Method conducting principle, hardware to be used, data interpretation manual with IT solutions developed with appropriate criteria;
2. Detailed description of the variations included;
3. Analytical sensitivity and specificity verification documentation;
4. Stability study data;
5. Results of the Genterf preclinical trial, including more than 400 individuals with different reproduction-related phenotypes

A word mark "GENTERF", registration number M 75 588, date of registration 20.06.2020 was registered in addition.

In cooperation with one of the leading infertility clinics in Latvia, clinical performance studies of the GENTERF genetic test are currently being carried out, which will be concluded on 31 May 2022 and the results obtained will be transferred to the licensee without additional charge.

Topicality

Infertility is considered a major public health issue. Approximately 1 out of 6 people worldwide suffer from infertility during their lifespans. Currently, the diagnostic timeline of infertile couples includes biochemical and instrumental analyses that allow for a diagnosis in 65% of cases; in the remaining 35% of cases, which are undiagnosed, genetic tests are performed[1].

Rīga Stradiņš University (RSU) has developed GENTERF that allows the identification of known and most frequent clinically relevant genetic variations in both men and women, using a single test kit that can identify the most common genetic causes for genetic infertility and reproductive risk factors, genetic risk factors that can influence hormonal treatment and the status of carriers of the most common autosomal recessive diseases.

The method developed is based on human DNA analysis using a multiplex (multi-level) polymerase chain reaction with fluorescently-labelled synthetic oligonucleotides (primers) that allows multiple genetic variations to be detected at the same time. It requires a polymerase chain amplifier, capillary electrophoresis, which can determine the length of the fluorescent fragments and other standard molecular biology laboratory equipment (automatic pipettes, centrifuges, vortexes).

[1] Cariati, F., D'Argenio, V. & Tomaiuolo, R. The evolving role of genetic tests in reproductive medicine. *J Transl Med* **17,** 267 (2019). https://doi.org/10.1186/s12967-019-2019-8

Description of stages of development and results of GENTERF:

- The GENTERF test method has been developed by the RSU Scientific Laboratory of Molecular Genetics accredited in accordance with the corresponding ISO Medical Laboratory standard ISO15189:2012 (LATK-633-00-2020);
- Analytical sensitivity of the GENTERF test is >99% and specificity is > 99%;
- The GENTERF clinical trial plan has been prepared in accordance with ISO 20196:2019;
- The clinical performance study of the GENTERF genetic test has received the authorisation of the State Agency of Medicines, the identification number of the study in the European Database on Medical Devices EUDAMED is CIV-LV-20-12-035444;

For the determination of analytical sensitivity and specificity, 33 specifically selected DNA samples with as different genotypes as possible were analysed, so that three different genotypes, the normal and the rare allele for rarer variations could be tested. As far as possible, external quality control schemes proposed by accredited reference laboratories were also used to verify the performance of a developed method.

Benefits of GENTERF

- The genetic root cause of infertility can be diagnosed faster;
- Improved clinical decision-making;
- The possibility of adjusting treatment individually based on test results;
- Lower overall treatment costs due to faster diagnosis and targeted treatment;
- Lower risk of postnatal pathology, as testing for some carriers of hereditary autosomal recessive diseases is included.

* The intellectual property of Rīga Stradiņš University – know-how *"Innovative genetic test for determining the causes of infertility "Genterf""* was created within the scope of project No. KC-PI-2017/24 *"Genetic test for determining the causes of infertility"* of Activity 1.2.1.2 *"Support for Improvement of Technology Transfer System"* of Specific Objective 1.2.1 *"To increase Investments of Private Sector in R&D"* of the Operational Programme *"Growth and Employment"*.