

## Non-invasive genetic analysis to understand pregnancy loss

### PATIENT CONSENT FORM

**CLARITY is a non-invasive blood test that can be performed after a pregnancy loss.** The test analyses small fragments of DNA (called **cell-free DNA**) circulating in the mother's blood. This DNA comes from both the mother and the non-viable pregnancy. By analysing this genetic material, the test aims to identify chromosomal changes in the fetus that may have contributed to the miscarriage.

It is important to understand that the DNA in the blood sample is a mixture of maternal and fetal DNA. For this reason, the test may occasionally detect chromosomal changes originating from the mother, which may also be relevant for understanding the pregnancy outcome.

The test requires a blood sample taken **from a vein in the woman**. To obtain a reliable result, the sample should be collected **before the pregnancy tissue has passed** and when the pregnancy has reached at least **6 weeks of gestation**.

The test has high accuracy for detecting common chromosomal abnormalities, with 95% sensitivity for autosomal aneuploidies and over 99% sensitivity for sex chromosome abnormalities and fetal sex determination. The test's specificity is ≥85%. Test performance may vary depending on factors such as sample quality and the amount of fetal DNA in the blood.

CLARITY performs a **genome-wide** analysis enabling the detection of chromosomal abnormalities across all chromosomes. The test is intended to identify the following chromosomal conditions:

- **Autosomal aneuploidies**
- **Sex chromosome aneuploidies**
- **Fetal chromosomal sex**

#### RESULTS

CLARITY test results are sent to the clinician **within 10 working days** after the blood sample has arrived at the Celvia medical laboratory. The result and any need for follow-up testing must be explained to the patient by a doctor, midwife, or medical geneticist. The test can provide the following types of results:

#### Positive result

One or more chromosomal abnormalities have been detected. These findings may explain the cause of the miscarriage. The abnormality may originate from the retained fetal tissue or, in some cases, from maternal chromosomal changes. If a maternal origin finding is suspected, it will be indicated in the report.

#### Negative result

No chromosomal abnormalities were identified in the analysed sample. A negative result does not exclude a genetic cause of the miscarriage, as some abnormalities may fall outside the scope or detection limits of the method.

#### Non-informative result

In some cases, a result may not be obtained due to insufficient blood sample volume, early gestational age (<6 weeks), delayed or unsuitable sample transport, or issues with sample quality. In rare cases, technical limitations (e.g. high background noise) or errors in sample identification may also prevent analysis. The likelihood of a non-informative result is low (less than 1%).

#### METHODS

For the CLARITY test, a blood sample is collected into a special tube that preserves the DNA during transport to the laboratory. In the laboratory, plasma is separated from the blood, and the cell-free DNA is extracted. The test uses a method that increases the amount of pregnancy-related DNA in the sample to improve analysis accuracy.

The DNA is then analysed using advanced sequencing technology, NGS technology, which reads genetic information from across all chromosomes. Based on this information, the test assesses whether chromosomal abnormalities may be present.

#### LIMITATIONS

The CLARITY test is designed to detect the most common chromosomal abnormalities associated with pregnancy loss. However, it does not identify all genetic conditions, and test results should be interpreted together with clinical information.

Because the test analyses cell-free DNA (cfDNA) from the blood, some abnormalities may not be detected. Therefore, both false-negative and false-positive results are possible.

The test is not designed to detect:

- Triploidy or tetraploidy
- Single-gene (monogenic) disorders or point mutations
- Small chromosomal changes below the detection limit of the method
- Low-level or tissue-specific mosaicism
- Balanced chromosomal rearrangements (e.g. balanced translocations or inversions)
- Uniparental disomy

A normal (negative) result reflects only the DNA analysed in the blood sample and does not exclude all possible causes of pregnancy loss. The test does not provide information about fetal structural development and does not assess non-genetic causes, such as uterine, placental, or maternal factors.

**I confirm that I have read the information provided in this consent form and I agree to provide a blood sample for the CLARITY test.**

.....

Patient's signature

Date

### TEST ORDERING FORM

Fill it in only if you did not order electronically

First name and surname of the patient

Patient personal ID or date of birth

Type of sample?  BLOOD

Pregnancy week (example 8)

Date of blood sampling (dd/mm/yyyy)

I confirm that the blood sample was collected immediately after the ultrasound examination and that retained pregnancy tissue was present in the uterus at the time of sampling.

Clinician's name

Clinician's phone number

Clinician's e-mail

I confirm that I am ordering the CLARITY test at the patient's request. I confirm that the patient has been informed about the purpose, possible results, and limitations of the test. I confirm that the patient has provided informed consent and that the information provided is accurate and complete.

.....

Clinician's signature

Date