TEST REQUISITION FORM

PATERNITYSAFE
Non-Invasive Prenatal Paternity Test

Protocol No. (internal use only):_____

ORDERING LABORATORY / CLINICIAN

eurofins | Genoma

Dear customer,

Please read the instructions reported below carefully. The failure or incorrect compliance with the instructions could compromise the validity of the test.

FEMALE PARTNER

Name _____

Surname _____

Date of birth_____ Place of birth_____

Address_____

Gestational age (minimum 9 weeks + 0 days): _____

Pregnancy: ☐ single ☐ monochorionic twins

Transplants / transfusions ☐ yes ☐ no

(Personal data above are required for authorization purposes only and are processed and protected according to European Regulation 2016 / 679 (Personal Data Protection Code).

MALE PARTNER (ALLEGED FATHER)

Name _____

Surname _____

Date of birth_____ Place of birth_____

Address _____

(Personal data above are required for authorization purposes only and are processed and protected according to European Regulation 2016 / 679 (Personal Data Protection Code).

COLLECTION BOX

Inside the Shipping kit you will find:

- No. 1 Cell-free DNA BCT tubes of 10 mL (for maternal blood);
- No. 1 Adhesive label with barcode for the Cell-free DNA BCT tubes (for maternal blood);
- No. 1 buccal swab (for collection of the paternal sample);
- No. 1 adhesive label with barcode for the buccal swab (for the paternal sample);
- No.1 sponge mold for positioning the tubes once the sampling has been performed;
- Nr. 1 resealable zipper seal Biohazard bag.
- Nr. 1 white box containing the previously described material;
- Nr. 2 consent forms for the test requested;
- Nr. 1 instructions sheet.

PLEASE NOTE: do not use different tubes from those provided.

REPORTING PREFERENCES

☐ **PHYSICIAN / LABORATORY**

☐ **E-mail** _____

☐ **On-Line**

In order to activate the on-line reporting option, you need to provide us

Username _____ **Password** _____

Identifying personal password (mandatory):

_____

IMPORTANT: in the absence of the above-mentioned password, the laboratory will not be able to provide any information on the status of the requested exam and its outcome.

DATE _____

FEMALE PARTNER SIGNATURE

_____

MALE PARTNER SIGNATURE

_____

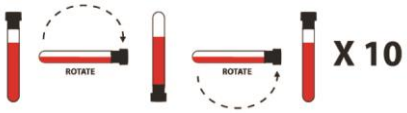
Test submission instructions (Maternal blood)

Informed consent and test requisition form

IMPORTANT: Fill in all required Test Requisition Form information to avoid delays and ensure timely reporting. To ensure acceptance of your patient's specimen for testing, please verify that the informed consent has been signed and it has been enclosed with samples.

Sample collection instructions

- Take the 10ml collection tube from the **PaternitySafe®** Test Shipper Kit.
- Write the **blood collection date** in the specimen information section of the test requisition form.
- Write the patient's **full name and date of birth** on the collection tube label.



- Fill the collection tube almost completely with whole blood.
- Invert the collection tube 10 times.

Store collected blood at **room temperature** until ready for shipment. **Blood should never be frozen!**

Sample Packaging and Shipping:

IMPORTANT: Always store kits at **room temperature**.

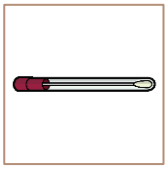
- Place the filled and properly labeled collection tube into the shipper kit box.
- Place the completed **test requisition form** and **informed consent** into the shipper kit box, at the side.
- Put sample tubes inside the sponge and both inside the biohazard envelope. Close the box.
- Place shipper kit box inside of courier pack and seal.
- If you are shipping more than one shipper kit, place as many as possible into one courier pack.
- Adhere the **courier airbill** pouch to the outside of the courier pack. Insert the airbill into the pouch.
- **Call courier** to arrange specimen pickup.
- Ship specimens, preferably the **same day** as collected. Specimens must be received by Genoma **within 5 days** of collection date. Genoma receives specimens Monday through Saturday.

Test Submission Instructions (Paternal DNA)

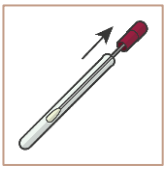
WARNING!

To properly perform the buccal cells collection procedure by buccal swab, it is important to comply with the follow recommendations 1h prior to the buccal cells collection:

- Do not eat
- Do not drink
- Do not smoke
- Do not chew gums
- Do not brush your teeth



1. Open the package.

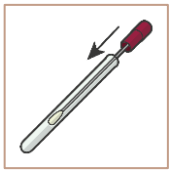


2. Pull out the swab from the test tube.

Warning! Do not touch the swab cotton part in order to avoid contamination!

3. It is advisable to rub the swab on both cheeks, and the inner lining of the lips.

4. Repeat the above procedure several times.
For a standard collection it is necessary to rub for at least 60 seconds.



5. Reinsert the swab into the test tube

6. Close the swab carefully.

7. Apply the label with the patient's full name and date of birth on the test tube.

8. Place the collection tube into the shipper kit box, together with the maternal blood sample.

PATIENT CONSENT FORM

Test Purpose

A non-invasive prenatal paternity test is a way to determine who the father is before the baby is born. While the mom is pregnant, the DNA profile of the baby is determined from free-floating fetal cells found in the mom's blood sample. The baby's profile is compared to the DNA profile of the man tested—his DNA is collected by a simple mouth swab. A report is then generated to show if the man tested is or is not the biological father. Until recently, the only way to test for paternity while pregnant was to collect amniotic fluid via a long needle, which is an "invasive" procedure that presents a risk to the baby. "Non-invasive" means there is no need to intrude in the baby's safe environment to test for paternity. Instead, we collect only a blood sample from the mom's arm, and a cheek-swab sample from the father.

How the PaternitySafe™ test is performed

The PaternitySafe™ test uses a state-of-the-art technological process, named Next Generation Sequencing (NGS) technique, to measure differential allele contributions in a panel of amplified SNPs.

The PaternitySafe™ test was performed to determine paternity using cell-free circulating fetal DNA (cfDNA) isolated from the plasma of the maternal blood sample. This sample contains a mixture of maternal and fetal DNA. Fetal fraction represents the percentage of fetal DNA found in the maternal blood. Fetal fraction increases as gestation time increases and decreases shortly after childbirth. If the maternal plasma does not contain a sufficient amount of fetal DNA, a result cannot be produced. DNA was also isolated from nucleated cells in the samples from the mother and alleged father. Fetal DNA isolated from the maternal blood, which contains placental DNA, DNA was also isolated from nucleated cells in the samples from the mother and alleged father, were amplified at specific loci using a targeted PCR assay, and sequenced using a high-throughput sequencer. All DNA samples were analyzed using a state-of-the-art technological process, named Next Generation Sequencing (NGS) technique. A panel of >500 SNP (Single Nucleotide Polymorphism) loci with high heterozygosity, low amplification error, low linkage, were selected for amplification and sequencing in NGS sequencers. Sequencing is performed at high resolution (sequencing depth >1000X, average 4000X). An analysis pipeline incorporating a proprietary NGS bioinformatics tools is used to align reads to the SNP regions and determine parentage, comparing the DNA profile of the fetus's DNA to the DNA profile of the possible father. Afterwards a probability of paternity was generated Calculations for the Probability of Paternity were performed using a proprietary algorithm.

Results of the PaternitySafe™ test

COMPATIBILITY: free circulating fetal DNA is compatible with the alleged father's DNA when the examination of the polymorphic regions investigated in the non-invasive paternity test detects its presence in both samples. This result is compatible with an attribution of paternity within the limits of the method.

NON COMPATIBILITY: free circulating fetal DNA is not compatible with the alleged father's DNA when the polymorphic regions of the son and the alleged father, investigated in the non-invasive paternity test, differ. This result is compatible with an exclusion of paternity within the limits of the method.

In both cases, although the risk of test error is low (<1%), it cannot be excluded. The result can be confirmed in the pre-natal phase by invasive procedures (CVS / amniocentesis) or in the post-natal phase using traditional techniques.

The result of the test does not provide for the issue of genetic profiles in association with the report

In some cases (about 1%) the test may produce a non-optimal or inconclusive result. In such cases, the pregnant woman will be asked to take a new blood sample in order to repeat the test. Even after repetition, the test may produce an inconclusive result

PaternitySafe™: Limitations

As with all tests performed on cffDNA, the PaternitySafe is to be considered a screening test and although the exam has shown, in preclinical validation studies, a reliability of more than 99%, the risk of test error cannot be excluded.

The test can be performed on monozygotic single or twin pregnancies, with at least 9 weeks of gestation. For technical reasons, the test cannot be performed if the presumed fathers are monozygotic twins, if the pregnancy is bicorial twins or if the pregnancy is obtained from MAP with heterologous female fertilization and the donor collection is not available.

In pregnancies that began as dizygotic or multiple twins, followed by the spontaneous abortion of one or more fetuses with resorption of the gestational chamber (vanishing twin), the DNA of the aborted fetus may also be present in the maternal blood. This could interfere with the quality of the results.

Discordant test results may occur due to one or more of the following rare events: Biological factors, such as too low an amount of fetal DNA (Fetal Fraction) in the maternal blood sample, vanishing twin, an undetected dizygotic twin pregnancy, previous transplant organ, blood transfusions, or other causes. The ability to report results may be affected by maternal body mass index (BMI), maternal weight and / or maternal systemic lupus erythematosus (SLE).

Maternal plasma contains variable percentages of FF (fetal fraction), which differ in different samples. The LoD (Limit of Detection) that is the percentage of fetal DNA below which the test cannot be performed is 2%. In some cases, the analyzed sample may show a low fetal fraction (<2%) and consequently the test may lead to an inconclusive result. In such cases, a new blood sample will be required in order to repeat the examination in a more advanced gestational age. Even in this case, it is not excluded that, even after repeating the survey, the test may again lead to an inconclusive result.

Reporting times

The results will be available in more than 15 days from the sample reception. However, these terms can be prolonged in case of test repetition or not conclusive results.

Use of Information and Leftover Specimens.

Pursuant to best practices and clinical laboratory standards leftover de-identified specimens (unless prohibited by law) as well de-identified genetic and other information learned from your testing may be used by Genoma or others on its behalf for purposes of quality control, laboratory operations, laboratory test development, and laboratory improvement. All such uses will be in compliance with applicable law.

PATIENT CONSENT STATEMENT:

By signing this form, I, the patient having the testing performed, acknowledge that:

- I have received and read or have had read to me the above informed consent information about the PaternitySafe™ test in its entirety and realize I may retain a copy for my records;.
- I have had the opportunity to ask questions of my health care provider regarding this test, including the reliability of test results, the risks, and the alternatives prior to my informed consent.;
- I have been informed about the availability and importance of genetic counseling and have been provided with information identifying an appropriate healthcare provider from whom I might obtain such counseling;
- I consent to the use of the leftover specimen and health information as described in the Patient Informed Consent;
- I consent to having this test performed and I will discuss the results and appropriate medical management with my healthcare provider.

DATE_____

FEMALE PARTNER SIGNATURE _____ MALE PARTNER SIGNATURE_____