Ninalia
by eurofins biomnis

Information and Consent Form

Non-invasive Prenatal Testing (NIPT) for trisomies 21, 18 and 13

Three copies of this document should be drawn up (patient, prescribing physician, Eurofins Biomnis Laboratory).

This genetic test to screen for trisomies 21, 18 and 13 is based on the study of fœtal DNA circulating in the mother's blood. This test is indicated in pregnant women situated in a high-risk group of giving birth to a fœtus with Trisomy 21,18 or 13. Performed thanks to new generation sequencing technology, this screening test using free, circulating DNA only requires a simple blood test without any risk to the fœtus. The test can be performed **as of week 10 of pregnancy (= 12 weeks of amenorrhea)**. It is essential that all positive results are confirmed by an invasive test to confirm the diagnosis. This test falls within the scope of prenatal screening and the pregnant woman should receive accurate and full information (L2131-1 of the Public Health Code).

TEST RECOMMENDATIONS

This genetic test is proposed for patients in an at-risk group according to the following recommendations:

- **Patients in an at-risk group after evaluation of maternal serum markers: risk higher than or equal to 1/1000 without increased nuchal translucency or other ultrasound abnormality.**
  - Combined screening in the first trimester - *Attach the copy of the result*
  - Integrated sequential screening in the second trimester - *Attach the copy of the result*
  - Screening in the second trimester for serum markers alone - *Attach the copy of the result*
- **History of pregnancy with trisomy 21, 18 or 13** - *Attach the copy of the result*
- **Couple where one of the members carries a Robertsonian translocation involving chromosomes 13 or 21** - *Attach the copy of the result*
- **For twin pregnancies without high nuchal translucency (nuchal translucency < 3.5 mm) or other abnormalities** - *Please attach a copy of the ultrasound report*
- **For patients aged 38 years or more that were not able to perform the maternal serum markers test**
- **Unreliable maternal serum markers results (serum markers with borderline values)**

Recommendations:

According to recommendations from French Health Authorities (HAS) and International (ACOG) learned society, this test is not recommended in cases where there are ultrasound anomalies or in cases where the nuchal translucency is greater or equal to 3.5 mm.

If an enlarged nuchal translucency, an obvious anomaly or a cystic hygroma is identified on ultrasonography, the patient should be offered genetic counseling and diagnostic testing for aneuploidy as well as follow-up ultrasonography for fetal structural abnormalities.

Observation:

- The first trimester ultrasound remains essential to:
  - date the pregnancy;
  - measure nuchal translucency;
  - detect multiple pregnancies;
  - detect congenital abnormalities other than nuchal translucency.

INTERPRETATION

- For a cohort of 3107 patients (data from the supplier Illumina, Feb. 2017):
  For Trisomy 21, the sensitivity of this test is 98.9% and the specificity is > 99.9%.
  For Trisomy 18, the sensitivity of this test is 90% and the specificity is 99.9%.
  For Trisomy 13, the sensitivity of this test is > 99% and the specificity is 99.9%.
  Nonetheless, a negative result does not fully exclude the existence of specifically tested or other abnormalities.
  Consequently, it is essential to follow up rigorously with morphological ultrasounds.
- A positive result does not necessarily mean that the fœtus carries trisomy 21, 18 or 13. It is essential that all positive results are confirmed by an invasive test. The fœtal karyotype is the only examination which enables the confirmation of a Trisomy 21, 18 or 13 diagnosis.

Observation:

The failure rate of this test is limited: a result cannot be obtained, essentially in women with a very high body mass index. It limits the detection of fœtal fraction.

LIMITATIONS

This test does not detect:

- unbalanced translocations, microdeletions, microduplications;
- mutations causing other diseases;
- neural tube abnormalities;
- cases of triploidy

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PATIENT INFORMATION AND CONSENT FORM

I, the undersigned .....

▸ **hereby certify that I have received, from the doctor *(name, surname):*** .....

in accordance with article L2131-1 of the Public Health Code, during a medical consultation dated D D M M Y Y

1. Information in regard to:

- the risk to the child of being born with a condition of particular severity, in particular trisomy 21, 18 or 13;
- the possibility at my request of having recourse to either an invasive procedure (amniocentesis or chorial villosity biopsy) with a view to preparing a foetal karyotype, or Non-invasive Prenatal Testing for trisomies 21,18 and 13.

2. Moreover, I have received the following information on Non-invasive Prenatal Testing for trisomies 21, 18 and 13 which I would like to take advantage of:

- A blood test is performed as of week 10 of pregnancy (= 12 weeks of amenorrhea), without any risk to my fœtus.
- This test detects trisomies 21, 18 and 13.
- Optional: this test can also detect sex chromosomes aneuploidies [1] and gender
- The result will be sent to me and explained by the prescribing physician or another practitioner experienced in prenatal screening.
- This is a screening test and does not in itself enable a diagnosis to be made.
- Nonetheless, a negative result does not fully exclude the existence of specifically tested or other abnormalities. Consequently, it is essential to follow up rigorously with morphological ultrasounds from the second and third trimesters.
- A positive result does not necessarily mean that the fœtus carries trisomy 21, 18 or 13. Due to false positive results, any positive result should be followed by a genetic conselling and by an amniocentesis with the aim of performing a fœtal karyotype, the only examination that enables confirmation of the diagnosis of trisomy 21, 18 or 13. The risks, restrictions and possible consequences of each sample technique will be explained to me.
- Any conditions other than those specifically tested initially could be revealed by the examination.
- I have been informed of the price of this test and I am aware that I may have to partially or fully pay the cost of the test myself, depending on my health insurance cover.

I hereby consent to the performing of Non-invasive Prenatal Testing of trisomies 21, 18 and 13.

In accordance with prevailing texts, my sample will be removed once the legal storage period has expired or once used by Eurofins Biomnis Laboratory; this will be anonymous and in compliance with medical confidentiality for scientific or quality assurance purposes. I can object to this use by sending a regular mail addressed to Eurofins Biomnis for the attention of the medical secretariat.

This screening will be performed by Eurofins Biomnis Laboratory, a medical biology laboratory authorised by the Regional Public Health Authority to perform prenatal diagnosis.

The original copy of this document will be stored in my medical record by the prescribing physician.

A copy of this document will be sent to me.

The second copy will be sent to Eurofins Biomnis Laboratory, which will perform the test. They will store this document under the same conditions as the examination report.

Date: D D M M Y Y

[1] There is limited data available on sex chromosomes aneuploidies (Monosomy X, XXX, XXY, XYY) and additional information is not currently available

Prescribing clinician's signature	**Patient's signature**

This document was drawn up based on recommendations from:
- the American College of Obstetricians and Gynecologists (ACOG), Sept 2015
- Decree 2014-32 of 14 January 2014
- HAS, May 2017 (French Health Authorities)

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