Prenatalsafe®

eurofins | Genoma

NON-INVASIVE PRENATAL TESTING

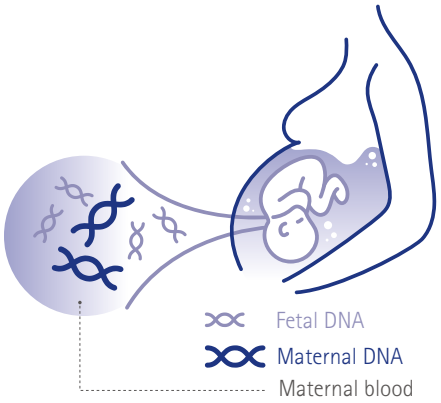
NIPT

Non-invasive prenatal testing (NIPT), since its introduction into clinical practice over 10 years ago, has positively influenced prenatal diagnosis[1]. NIPT has established itself as a safe alternative to invasive investigations (i.e., amniocentesis and villocentesis), while ensuring high reliability in relation to serological tests such as the Bi-test.

Recommended for **all pregnant women**

HOW DOES **NIPT WORK**?

It is a non-invasive test that allows studying fetal genetic material with a simple blood sample from the mother.



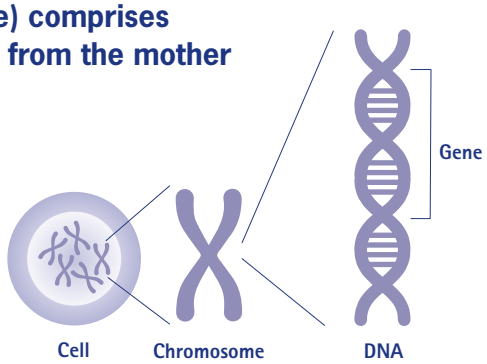
The test can detect and analyse fetal DNA circulating in maternal blood to **identify the presence of chromosomal abnormalities and genetic diseases in the fetus**.

The amount of fetal DNA increases during pregnancy and **from week 10 of gestation is adequate for screening**. If this quantity is not reached, a second sampling may be recommended.

The chromosome set (called a karyotype) comprises 23 pairs of chromosomes, half inherited from the mother and half from the father:

- **22 pairs of non-sex chromosomes**
- **1 pair of sex chromosomes**

Chromosomes are formed from DNA. Some DNA segments are defined as GENES and provide the cell with the information required to perform its function.



Abnormalities in the delicate process that leads to the formation of gametes can cause **different types of alterations**:

- **Abnormalities in the number of chromosomes: ANEUPLOIDIES**
- **Abnormalities in the structure of CHROMOSOMES**

Variations in the DNA sequence called genetic mutations can occur. This kind of alteration may be inherited from parents, or occur for the first time in the fetus and cause:

- **Genetic DISEASES**

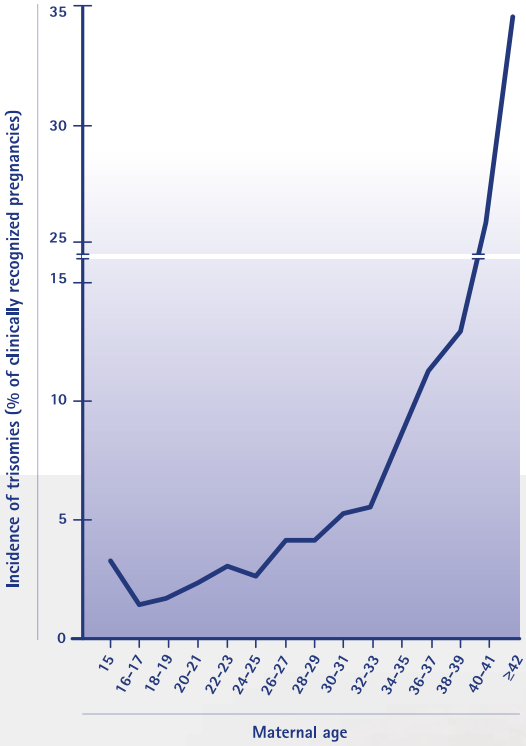
The frequency of these alterations increases mainly with maternal age, but also advanced paternal age may be a risk factor.

WHAT CAN BE INVESTIGATED
WITH NIPT?

1) Abnormalities in the number of chromosomes: ANEUPLOIDIES

TRISOMY: three copies of a chromosome

MONOSOMY: single copy of a chromosome



Among the most common ones[2]:

- **Trisomy of chromosome 21 (Down Syndrome):** 1 in 700 births
- **Trisomy of chromosome 18 (Edwards Syndrome):** 1 in 3.000 births
- **Trisomy of chromosome 13 (Patau Syndrome):** 1 in 6.000 births

Incidence increases with increasing maternal age[3].

2) Abnormalities in the structure of CHROMOSOMES

DELETION: loss of a chromosome segment

DUPLICATION: doubling of a chromosome segment

If these rearrangements are very small, they are called microdeletions and microduplications.

Microdeletion 22q11.3 is the most frequent microdeletion and is linked to DiGeorge syndrome, which has an incidence of 1/2.000–4.000 people, regardless of maternal age[4].

3) Genetic DISEASES

***DE NOVO*:** caused by DNA mutations that occur for the first time in the fetus

HEREDITARY: caused by mutations inherited from parents

It is important to test specifically for the possibility of being a HEALTHY CARRIER*.

***Healthy carrier**, that is one who can transmit the disease but is not affected and therefore has no symptoms.

Prenatalsafe®

Over 20 years of experience in genetic testing. Prenatalsafe® ensures accurate testing of circulating fetal DNA to investigate the presence of:

- Aneuploidies in all the chromosomes of the fetus
- Deletions and duplications on all chromosomes (>7Mb)
- 9 microdeletion syndromes
- Inherited and *de novo* genetic diseases

AN OFFER FOR EVERY NEED

	3	5	5DiGeorge	Plus	Karyo	Karyo Plus	Complete	Complete Plus	Full Risk
Fetal sex	●	●	●	●	●	●	●	●	●
Trisomy 21 Down Syndrome	●	●	●	●	●	●	●	●	●
Trisomy 18 Edwards Syndrome	●	●	●	●	●	●	●	●	●
Trisomy 13 Patau Syndrome	●	●	●	●	●	●	●	●	●
Sex Chromosome Aneuploidies		●	●	●	●	●	●	●	●
Rare Autosomal Aneuploidies				9 and 16	●	●	●	●	●
Deletions and Duplications					●	●	●	●	●
Microdeletions			22q11.2	●		●		●	●
Inherited genetic diseases							●	●	●
***De novo* genetic diseases**							●	●	●
Carrier screening test*									●

***Testing on both parents** to see whether they carry mutations related to 30 of the most common genetic diseases in the Italian population

- **Free pre-test genetic counselling**

to identify the suitable level for the couple's needs

- **Free post-test genetic counselling**

if positive

Microdeletions:

	Microdeletion Syndromes	Chromosome regions
Prenatalsafe® 5DiGeorge	DiGeorge Syndrome	deletion 22q11.2
Prenatalsafe® Plus	includes Prenatalsafe® 5DiGeorge +	
	Cri-du-chat Syndrome	deletion 5p15.3
	Prader-Willi Syndrome	deletion 15q11.2
	Angelman Syndrome	deletion 15q11.2
	1p36 Deletion Syndrome	deletion 1p36
	Wolf-Hirschhorn Syndrome	deletion 4p16.3
Prenatalsafe® Karyo Plus	includes Prenatalsafe® Plus +	
	Jacobsen Syndrome	deletion 11q23
	Langer-Giedion Syndrome	deletion 8q24.11-q24.13
	Smith-Magenis Syndrome	deletion 17p11.2

Inherited genetic diseases:

- CFTR Cystic Fibrosis
- CX26 (GJB2) Deafness Autosomal Recessive Type 1A
- CX30 (GJB6) Deafness Autosomal Recessive Type 1B
- HBB Beta Thalassemia
- HBB Sickle Cell Anemia

De novo genetic diseases:

Syndromic Disorders

Alagille Syndrome	JAG1
CHARGE Syndrome	CHD7
Cornelia de Lange Syndrome, type 5	HDAC8
Cornelia de Lange Syndrome, type 1	NIPBL
Rett Syndrome	MECP2
Sotos Syndrome, type 1	NSD1
Bohring-Opitz Syndrome	ASXL1
Schinzel-Giedion Syndrome	SETBP1
Holoprosencephaly	SIX3

Noonan Spectrum Disorders

Cardiofaciocutaneous Syndrome, type 1	BRAF
Noonan Syndrome-like disorder with or without juvenile myelomonocytic leukemia (NSLL)	CBL
Noonan Syndrome, type 3	KRAS
Cardiofaciocutaneous Syndrome 3	MAP2K1
Cardiofaciocutaneous Syndrome 4	MAP2K2
Noonan Syndrome, type 6	NRAS
Noonan Syndrome, type 1 LEOPARD Syndrome 1	PTPN11
Noonan syndrome, type 5 LEOPARD Syndrome 2	RAF1
Noonan syndrome, type 8	RIT1
Noonan syndrome-like disorder with loose anagen hair	SHOC2
Noonan syndrome, type 4	SOS1

Skeletal Disorders

Achondrogenesis, type II	COL2A1
Achondroplasia	FGFR3
CATSHL Syndrome	
Crouzon syndrome with acanthosis nigricans	
Hypochondroplasia	
Muenke syndrome	
Thanatophoric dysplasia, type I	
Thanatophoric dysplasia, type II	COL1A1
Ehlers-Danlos syndrome, classic	
Ehlers-Danlossyndrome, type VIIA	
Osteogenesi imperfecta, type I	
Osteogenesi imperfecta, type II	
Osteogenesi imperfecta, type III	
Osteogenesi imperfecta, type IV	
Ehlers-Danlos Syndrome cardiac valvular form	COL1A2
Ehlers-Danlos, type VIIB Syndrome	
Osteogenesi imperfecta, type II	
Osteogenesi imperfecta, type III	
Osteogenesi imperfecta, type IV	

Craniosynostosis

Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis	FGFR2
Apert Syndrome	
Crouzon Syndrome	
Jackson-Weiss Syndrome	
Pfeiffer Syndrome, type 1	
Pfeiffer Syndrome, type 2	
Pfeiffer Syndrome, type 3	

Prenatalsafe®

QUALITY PROVEN

LATEST GENERATION CE-IVD TECHNOLOGY

+

PROPRIETARY CE-IVD NIPT FLOW™ ALGORITHM

Sensitivity and specificity > 99%
demonstrated on 71.740 pregnancies

	Sensitivity (95% CI)	Specificity (95% CI)
Main Aneuploidies		
Trisomy 21	**99.54%** (98.36% - 99.94%)	**100%** (96.11% - 100.00%)
Trisomy 18	**100%** (96.11% - 100.00%)	**100%** (99.99% - 100.00%)
Trisomy 13	**100%** (90.51% - 100.00%)	**99.99%** (99.98% - 100.00%)
Sex chromosome aneuploidies		
X0	**98.11%** (89.93% - 99.95%)	**99.98%** (99.97% - 99.99%)
XXX	**100%** (87.23% - 100.00%)	**100%** (99.99% - 100.00%)
XXY	**100%** (86.77% - 100.00%)	**99.99%** (99.99% - 100.00%)
XYY	**100%** (86.77% - 100.00%)	**99.99%** (99.99% - 100.00%)
Rare Autosomal Aneuploidies, deletions, duplications and microdeletions		
Rare Autosomal Aneuploidies	**100%** (89.42% - 100.00%)	**99.92%** (99.89% - 99.95%)
Deletions and Duplications	**100%** (83.16% - 100.00%)	**99.97%** (99.96% - 99.99%)
Microdeletions	**83.33%** (35.88% - 99.58%)	**99.99%** (99.99% - 100.00%)

High sample validation

- Analysis of over **70.000 samples** for common trisomies
- Over **65.000 samples** for sex chromosome aneuploidies
- Over **40.000 samples** for other abnormalities

Reliability on all abnormalities

almost comparable to invasive investigation

First test in Italy with validation on large numbers for searching for Rare Autosomal Aneuploidies (RAA), segmental abnormalities (deletions and duplications) and microdeletions

GENETICS AT THE SERVICE OF CLINICAL PRACTICE

Prenatalsafe®, combined with an accurate ultrasound investigation, allows early identification of fetal abnormalities.

QUALITY CERTIFIED

MED N° 0018 M

GenQA certification

Aligned with the SIGU[5] guidelines, of the Ministry of Health[6] and with the main gynaecological **guidelines**[7]

11 geneticists supporting couples to offer pre- and post-test genetic counselling

Customer care available at any time on the path, from counselling to reporting

Logistics authorized for transporting biological material UN3373

Sample traceability

Comprehensive insurance protection

Bibliography

1. Non invasive prenatal testing (NIPT) for common aneuploidies and beyond. Eur J Obstet Gynecol Reprod Biol 2021 Mar;258:424-429

2. Screening for Fetal Chromosomal Abnormalities. ACOG Practice Bulletin, Number 226. Obstetrics & Gynecology: October 2020 - Volume 136 - Issue 4 - p e48-e69

3. To err (meiotically) is human: the genesis of human aneuploidy. Nature Reviews Genetics volume 2, pages280–291 (2001)

4. Cell-free DNA screening for prenatal detection of 22q11.2 deletion syndrome. Maternal and Fetal Medicine, held virtually, January 25–30, 2021

5. Pre-test counselling checklist for non-invasive prenatal genetic testing on fetal DNA circulating in maternal blood (NIPT/cell-free DNA test). 2021

6. Supreme Health Council Section I – Non-invasive screening of fetal DNA (NIPT) in public health. 2021.

7. SIEOG 2021 guidelines for obstetric and gynaecological ultrasound scans

YOUR PATIENTS **IN SAFE HANDS**

9 levels of investigation

- Accreditation as per UNI EN ISO 15189:2013 requirements
- CE-IVD NIPT FLOW™ ALGORITHM
- Illumina CE-IVD technology
- Qualified logistics

WHO IS IT FOR?

Any expectant mother, single or twin pregnancies, obtained with either natural conception or MAP techniques, autologous and heterologous.

Reporting times:

3-7 days	**10-15 days**	**15-20 days**
chromosome analysis	gene analysis	carrier testing on parents

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