

 Prenatal safe®



 eurofins

NON-INVASIVE PRENATAL TESTING

NIPT

Since the introduction of Non-invasive prenatal testing (NIPT) into clinical practice over 10 years ago, the clinical utility of prenatal screening has considerably improved. NIPT has become a safe alternative to invasive procedures such as amniocentesis and chorionic villus sampling in certain cases, while ensuring high sensitivity and specificity.

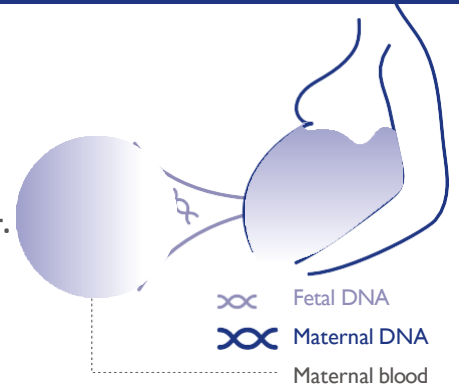


Recommended for **pregnant women with singleton and twin pregnancies**

HOW DOES NIPT WORK?

NIPT is a non-invasive test that enables the analysis of fetal genetic material from a routine blood sample taken from the mother.

The test can detect the presence of certain chromosomal abnormalities and genetic diseases in the fetus.

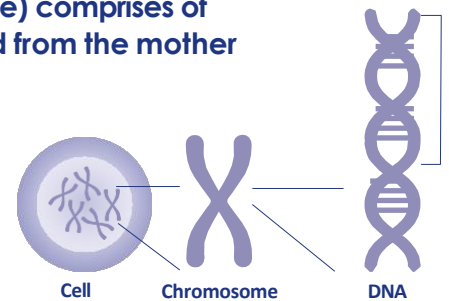


The amount of fetal DNA increases as pregnancy progresses and is adequate for screening from week 10 of gestation. If the quantity of fetal DNA is insufficient, a second sample may be required.

The chromosome set (called a karyotype) comprises of 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 regions are classified as GENES that provide the cell with the information required perform its function.



Abnormalities in the delicate process that leads to the formation of a developing fetus can cause different types of alterations:

- Abnormalities in the number of chromosomes: ANEUPLOIDIES
- Abnormalities in the structure of chromosomes: DELETIONS/DUPLICATIONS



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 advanced paternal age can also be a risk factor.

WHAT CAN BE INVESTIGATED WITH NIPT?

1) Abnormalities in the number of chromosomes: ANEUPLOIDIES

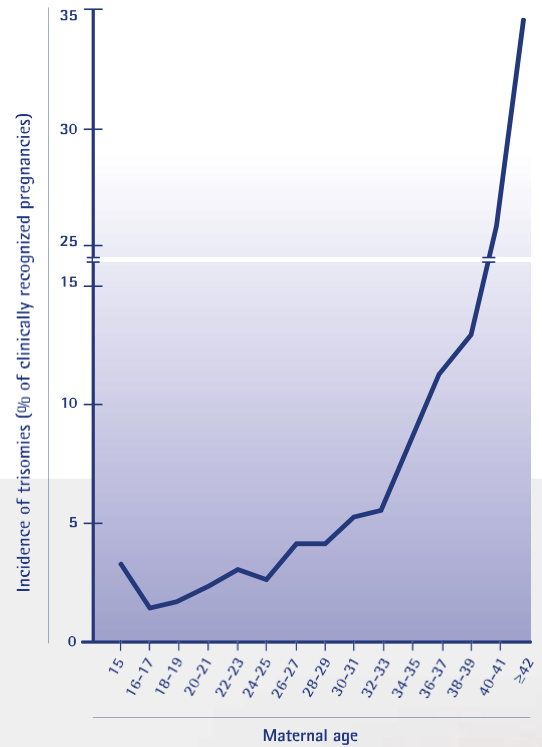
TRISOMY: three copies of a chromosome (instead of two)

MONOSOMY: single copy of a chromosome (instead of two)

The most common trisomys¹:

- Trisomy of chromosome 21 (Down Syndrome): 1 in 700 births
- Trisomy of chromosome 18 (Edwards Syndrome): 1 in 3000 births
- Trisomy of chromosome 13 (Patau Syndrome): 1 in 6000 births

Incidence increases with increasing maternal age².



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 1/2000–4000 people, regardless of maternal age³.

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 if parents are **HEALTHY CARRIERS*** of genetic diseases.

***Healthy carrier**, a person who is not affected by a disease and does not have symptoms, but has genetic sequences that mean the disease may be passed on to the fetus

Over 20 years of experience in genetic testing.
Prenatalsafe® can accurately test 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 UK*	5 UK*	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							●	●	●
<i>De novo</i> genetic diseases							●	●	●
Carrier screening test									●

*PrenatalSAFE 3 & 5 screens will be processed in the UK by Eurofins Clinical Diagnostics Lab, 8 Huxley Road, Guildford, GU2 7RE. All other screens will be referred to Genoma Labs, Italy.

- Free post-test genetic counselling if positive



Microdeletions

	Microdeletion Syndromes	Chromosome regions
PrenataSafe® 5DiGeorge	DiGeorge Syndrome	deletion 22q11.2
PrenataSafe® Plus	includes PrenataSafe® 5DiGeorge + Cri-du-chat Syndrome Prader-Willi Syndrome Angelman Syndrome 1p36 Deletion Syndrome Wolf-Hirschhorn Syndrome	deletion 5p15.3 deletion 15q11.2 deletion 15q11.2 deletion 1p36 deletion 4p16.3
PrenataSafe® Karyo Plus	includes PrenataSafe® Plus + Jacobsen Syndrome Langer-Giedion Syndrome Smith-Magenis Syndrome	deletion 11q23 deletion 8q24.11-q24.13 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		Skeletal Disorders	
Alagille Syndrome	JAG1	Achondrogenesis, type II	COL2A1
CHARGE Syndrome	CHD7	Achondroplasia	FGFR3
Cornelia de Lange Syndrome, type 5	HDAC8	CATSHL Syndrome	
Cornelia de Lange Syndrome, type 1	NIPBL	Crouzon syndrome <small>with acanthosis nigricans</small>	
Rett Syndrome	MECP2	Hypochondroplasia	
Sotos Syndrome, type 1	NSD1	Muenke syndrome	
Bohring-Opitz Syndrome	ASXL1	Thanatophoric dysplasia, type I	
Schinz-Giedion Syndrome	SETBP1	Thanatophoric dysplasia, type II	COL1A1
Holoprosencephaly	SIX3	Ehlers-Danlos syndrome, classic	
Noonan Spectrum Disorders		Ehlers-Danlos syndrome, type VIIA	
Cardiofaciocutaneous Syndrome, type 1	BRAF	Osteogenesis imperfecta, type I	
Noonan Syndrome-like <small>disorder with or without juvenile myelomonocytic leukemia (NSLL)</small>	CBL	Osteogenesis imperfecta, type II	
Noonan Syndrome, type 3	KRAS	Osteogenesis imperfecta, type III	
Cardiofaciocutaneous Syndrome 3	MAP2K1	Osteogenesis imperfecta, type IV	
Cardiofaciocutaneous Syndrome 4	MAP2K2	Ehlers-Danlos Syndrome <small>cardiac valvular form</small>	COL1A2
Noonan Syndrome, type 6	NRAS	Ehlers-Danlos, type VIIB Syndrome	
Noonan Syndrome, type 1 <small>LEOPARD Syndrome 1</small>	PTPN11	Osteogenesis imperfecta, type II	
Noonan syndrome, type 5 <small>LEOPARD Syndrome 2</small>	RAF1	Osteogenesis imperfecta, type III	
Noonan syndrome, type 8	RIT1	Osteogenesis imperfecta, type IV	
Noonan syndrome-like <small>disorder with loose anagen hair</small>	SHOC2	Craniosynostosis	
Noonan syndrome, type 4	SOS1	Antley-Bixler syndrome <small>without genital anomalies or disordered steroidogenesis</small>	FGFR2
		Apert Syndrome	
		Crouzon Syndrome	
		Jackson-Weiss Syndrome	
		Pfeiffer Syndrome, type 1	
		Pfeiffer Syndrome, type 2	
		Pfeiffer Syndrome, type 3	

LATEST GENERATION CE-IVD TECHNOLOGY

PROPRIETARY CE-IVD NIPT FLOW™ ALGORITHM
Sensitivity and specificity > 99%
demonstrated on 71740 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%)

Robust clinical validation

- Analysis of over **70000** samples for common trisomies
- Over **65000** samples for sex chromosome aneuploidies
- Over **40000** samples for other abnormalities

Reliability on all abnormalities

Internal data from samples analysed at Eurofins Genoma Italy.

For data on Sensitivity and Specificity for PrenatalSafe 3 and 5 performed in the UK refer to Illumina's clinical validation:

https://support.illumina.com/content/dam/illumina-support/documents/documentation/chemistry_documentation/verise-q-nipt-v2/veriseq-nipt-solution-v2-package-insert-canada-200006957-00.pdf

**GENETICS AT THE SERVICE
OF CLINICAL PRACTICE**

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



Aligned with the SIGU⁵ guidelines, of the Ministry of Health⁶ and with the main gynaecological guidelines⁷



Geneticists available to couples for pre- and post-test genetic counselling



Customer care available from pre-test counselling to reporting



Logistics authorized for transporting biological material UN3373



Sample traceability



Comprehensive insurance protection

Bibliography

1. Screening for Fetal Chromosomal Abnormalities. ACOG Practice Bulletin, Number 226. Obstetrics & Gynecology: October 2020 - Volume 136 - Issue 4 - p e48-e69
2. To err (meiotically) is human: the genesis of human aneuploidy. Nature Reviews Genetics volume 2, pages280–291 (2001)
3. Cell-free DNA screening for prenatal detection of 22q11.2 deletion syndrome. Maternal and Fetal Medicine, held virtually, January 25–30, 2021
4. Pre-test counselling checklist for non-invasive prenatal genetic testing on fetal DNA circulating in maternal blood (NIPT/cell-free DNA test). 2021
5. SIEOG 2021 guidelines for obstetric and gynaecological ultrasound scans

YOUR PATIENTS IN SAFE HANDS

9 levels of investigation

- 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 assisted reproductive technologies (ART)



*Actual kit used may vary from the picture shown above

Reporting times:

3-7 days

chromosome analysis

10-15 days

gene analysis

15-20 days

carrier testing on parents

 **eurofins**

Genoma

 **eurofins**

Clinical Diagnostics

GeneticEnquiriesUK@biomnis.co.uk

www.prenatalsafe.co.uk

UK Lab

Eurofins Biomnis UK Ltd
8 Huxley Road,
Surrey Research Park,
Guildford,
GU2 7RE

Rome

Laboratories and Medical
Offices Registered headquarters
and Laboratory for Research
and Development in Molecular
Genetics

Via Castel Giubileo, 11 / 00138

Laboratory for Medical
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Counselling

Via Castel Giubileo, 62 / 00138