Prenatalsafe®

eurofins

NON-INVASIVE PRENATAL TESTING

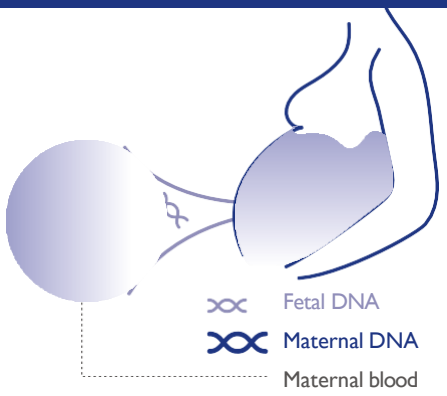
NIPT

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.



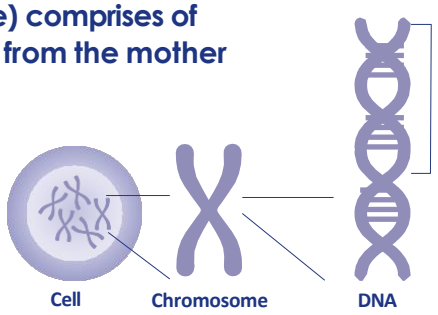
The test can detect **the presence of certain chromosomal abnormalities and genetic diseases in the fetus**.

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**

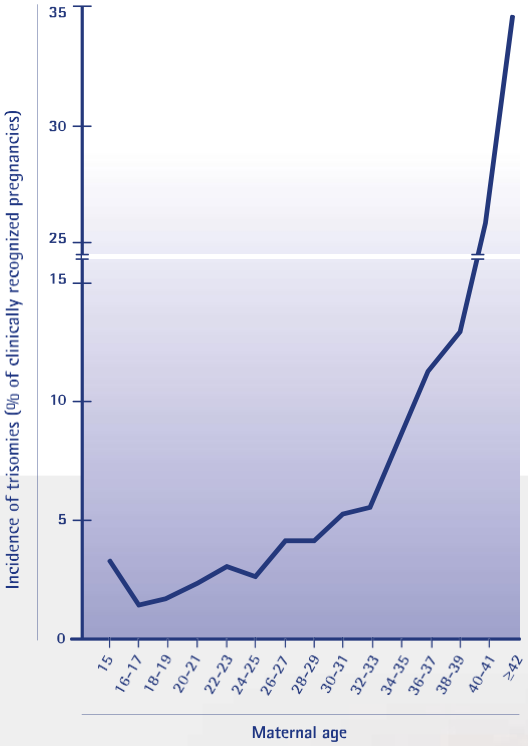
The frequency of these alterations increases mainly with maternal age, but advanced paternal age can also be a risk factor.

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 trisomys[1]:

- **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 age[2].

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 age[3].

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

Prenatalsafe®

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							●	●	●
De novo 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
Prenatalsafe® 5DiGeorge	DiGeorge Syndrome	deletion 22q11.2
Prenatalsafe® Plus	includes Prenatalsafe® 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
Prenatalsafe® Karyo Plus	includes Prenatalsafe® 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

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 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/veriseq-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.

Prenatalsafe®

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

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

*Actual kit used may vary from the picture shown above

WHO IS IT FOR?

Any expectant mother, single or twin pregnancies, obtained with either natural conception or assisted reproductive technologies (ART)

Reporting times:

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

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UK Lab

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Rome

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

Via Castel Giubileo, 11 / 00138

Laboratory for Medical Genetics and Molecular Diagnostics Sampling and Counselling

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