Cell-free fetal DNA analysis from maternal plasma that screens for genome-wide chromosomal abnormalities and severe genetics disorders in the fetus.
PrenatalSafe® test is the most technologically advanced NIPT. Through analysis of circulating cell-free fetal DNA (cfDNA) in maternal blood, it screens for genome-wide chromosomal abnormalities and severe genetic disorders in the fetus.

PrenatalSafe® test has a less than 0.1% false-positive rate for trisomies 21, 18, and 13. With conventional screening, as many as 1 in 20 women will receive a false-positive result. PrenatalSafe® test has exceptional accuracy, resulting in a detection rate greater than 99%. Conventional screening tests can miss 15% or more of trisomy 21 cases.
PrenatalSafe® COMPLETE represents the evolution of NIPT. It works as a complementary screen to traditional and genome-wide NIPT PrenatalSafe® Kayro. PrenatalSafe® COMPLETE also screens for several life-altering genetic disorders that are not screened with current NIPT technology, allowing a complete picture of the risk of a pregnancy being affected by a genetic disorder.
PrenatalSafe® Karyo PLUS IDENTIFIES 95.5% OF CHROMOSOMAL ABNORMALITIES PRENATALLY DETECTED²

Prevalence of fetal chromosomal aneuploidies detected by conventional cfDNA screening

- 52.9% Trisomy 21
- 13.3% Trisomy 18
- 5.2% Trisomy 13
- 7.5% Monosomy X
- 4.6% Sex Chromosome trisomy
- 16.9% Chromosomal abnormalities not detected

Prevalence of additional fetal chromosomal anomalies detected by PrenatalSafe® Karyo

- 16% Additional chromosomal anomalies detected by PrenatalSafe® Karyo
- 4.2% Satellites
- 2.9% Robertsonian translocations
- 2.1% Robertsonian rearrangements
- 1.6% Inversions
- 1.0% Deletions
- 0.6% Triplex
- 0.6% Mosaics
- 0.5% Mosaics
- 0.1% Mosaics
- 0.2% Other

Unlike any other non-invasive prenatal test (NIPT) available to date, PrenatalSafe® Karyo offers a level of information previously only available from a fetal karyotype analysis performed with invasive prenatal diagnosis procedures (amniocentesis and CVS).

<table>
<thead>
<tr>
<th>Traditional Karyotyping</th>
<th>PrenatalSafe® Karyo</th>
<th>PrenatalSafe® Karyo Plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analyses every chromosome</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects chromosomal gains ≥ 7 Mb</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects chromosomal gains ≥ 10 Mb</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Does not require an invasive procedure</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects additional translocations</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects segmental deletions/duplications</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects reciprocal translocations</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects marker chromosomes</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects microdeletions syndromes</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Detects triploidy</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Considered diagnostic</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>


² PrenatalSafe® Karyo PLUS identifies 95.5% of chromosomal abnormalities prenatally detected.
PrenatalSafe® Complete facilitates early diagnosis of single-gene disorders.

PrenatalSafe® Complete allows detection of common inherited genetic disorders in the fetus, that could be missed by traditional prenatal screening.

The inherited recessive disorders screened by PrenatalSafe® COMPLETE are the most common in the European population.

The inherited recessive disorders screened by PrenatalSafe® COMPLETE are:
- Cystic Fibrosis
- Deafness autosomal recessive type 1A
- Deafness autosomal recessive type 1B
- Beta-Thalassemia
- Sickle cell Anemia

De novo genetic conditions screened in the fetus

<table>
<thead>
<tr>
<th>Syndrome Disorders</th>
<th>Gene</th>
<th>Nevanen Spectrum Disorders</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usher syndrome 1A</td>
<td>USH1</td>
<td>Retinitis pigmentosa</td>
<td>RP1</td>
</tr>
<tr>
<td>Usher syndrome 1B</td>
<td>USH2</td>
<td>Retinitis pigmentosa</td>
<td>RP2</td>
</tr>
<tr>
<td>Usher syndrome 2A</td>
<td>USH3</td>
<td>Retinitis pigmentosa</td>
<td>RP3</td>
</tr>
<tr>
<td>Usher syndrome 2B</td>
<td>USH4</td>
<td>Retinitis pigmentosa</td>
<td>RP4</td>
</tr>
<tr>
<td>Usher syndrome 2C</td>
<td>USH5</td>
<td>Retinitis pigmentosa</td>
<td>RP5</td>
</tr>
</tbody>
</table>

The test detects de novo mutations in 25 genes causing 44 different genetic disorders. The genetic conditions screened by this innovative test are often present in the fetus in the absence of a family history of the condition. This is a paradigm shift in prenatal screening. PrenatalSafe® COMPLETE screens for de novo mutations that cannot be detected by standard carrier screening, as these mutations are not present in parents' somatic cells.

The genetic disorders screened can cause skeletal dysplasias, cardiac defects, multiple congenital anomalies, autism, epilepsy and/or intellectual disability.

**TEST CHARACTERISTICS**

**Simple**
A simple blood sample (8-10 ml) collected at 10+ weeks of gestation is required.

**Safe**
It is a non-invasive test, no risk for the fetus and the mother.

**Reliable**
Sensitivity and specificity >99%.

**Fast**
Turnaround time of just 3 days.

**Comprehensive**
It offers a level of information previously only available from a fetal karyotype analysis, performed with invasive prenatal diagnosis procedures (amniocentesis and CVS).

**Complete**
It detects both genome-wide chromosomal abnormalities and single-gene disorders, providing the most comprehensive information available from a noninvasive prenatal test to date.

**Useful**
The only genome-wide NIPT with a published prospective study demonstrating its clinical utility.

**Validated**
The only genome-wide NIPT with a clinical validation study performed on a cohort of over 12,000 pregnant women, with performance data published in prominent scientific journals.

**Advanced**
A groundbreaking technology allowing for a genetic analysis that is revolutionary.

**Global**
Prescribed by thousands of gynecologists worldwide.
**5 EASY STEPS**

Order the **Test**

Fill in and Sign Test Requisition and Consent Form

Draw a maternal blood sample (10 ml) at 10+ weeks of pregnancy

Call DHL on 0844 248 0844 to arrange collection of the sample, that is it!

**Receive results** in as little as 3 days

**SUPERIOR ACCURACY**

**High Resolution** sequencing: 
coverage ≈ 50 Millions of unique reads

**Exceptional performance:** Sensitivity and specificity >99%

**Accurate measurement of Fetal Fraction (FF)**

**Low limit of detection**: highly accurate at low cfDNA quantity (FF > 2%)

**Low incidence of inconclusive results**: (< 1%)
A GROUNDBREAKING TECHNOLOGY ALLOWING FOR A SCREENING TEST THAT IS REVOLUTIONARY

**Higher resolution**

PrenatalSafe® prenatal test uses more sequence reads than other NIPT’s (>50 Millions). More sequence reads equals higher resolution, greater sensitivity and precision.

**Accurate fetal fraction determination**

The test determines the quantity of cell-free fetal DNA (cfDNA) present in the maternal plasma (fetal fraction), and uniquely includes the analysis of cell-free DNA fragment size, allowing distinction between maternal and fetal cell-free DNA, for the highest accuracy.
DETECTS CHROMOSOMAL ABNORMALITIES AT LOW FETAL FRACTION (<4%)

Other NIPT approaches require a FF>4% for a reportable result.

A Genoma’s study\(^2\) demonstrated a six-fold increased incidence of aneuploidy (6.9% vs. 1.1%, p<0.001) in samples with 2%<FF<4% vs. samples with FF≥4%. These high risk pregnancies would have not been identified if the 4% FF cut-off had been used.

Samples at low FF are at higher risk of aneuploidy

An increased incidence (4-10 fold higher) of fetal aneuploidy has been reported in samples that failed to provide a reportable result from cfDNA testing due to low fetal fraction. This underscores the importance of testing samples with a very low amount of fetal cfDNA, using a NIPT method with a demonstrated accuracy at low FF, as PrenatalSafe\(^*\) prenatal test.

The ability to screen samples at low FF reduces the incidence of test cancellations and shortens the time required for the diagnosis of aneuploidy by invasive prenatal testing.

\(^2\)Fiorentino et al. The importance of determining the limit of detection of non-invasive prenatal testing methods. Prenat Diagn. 2016 Apr;36:304-11
PERFORMANCE YOU CAN RELY ON

<table>
<thead>
<tr>
<th></th>
<th>Trisomy 21 (n=36,192)</th>
<th>Trisomy 18 (n=36,192)</th>
<th>Trisomy 13 (n=36,192)</th>
<th>Monosomy X (n=36,192)</th>
<th>XXX (n=36,192)</th>
<th>XXXY (n=36,192)</th>
<th>SCA (n=36,192)</th>
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<tbody>
<tr>
<td>True positive</td>
<td>356</td>
<td>68</td>
<td>39</td>
<td>52</td>
<td>25</td>
<td>44</td>
<td>121</td>
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<tr>
<td>False positive</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
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<tr>
<td>True Negative</td>
<td>35,874</td>
<td>36,122</td>
<td>36,150</td>
<td>36,119</td>
<td>36,165</td>
<td>36,142</td>
<td>36,042</td>
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<tr>
<td>False Negative</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sensitivity (%) CI</td>
<td>99.99% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
</tr>
<tr>
<td>PPV (%) CI</td>
<td>99.99% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
<td>100.00% (99.98% - 100.00%)</td>
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</tr>
<tr>
<td>nPV (%) CI</td>
<td>100.00% (99.98% - 100.00%)</td>
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<td>100.00% (99.98% - 100.00%)</td>
</tr>
</tbody>
</table>

Performance PrenatalSafe: follow-up (May 2016)

<table>
<thead>
<tr>
<th></th>
<th>Trisomy 21 (n=11,932)</th>
<th>Trisomy 18 (n=11,932)</th>
<th>Trisomy 13 (n=11,932)</th>
<th>SCA (n=11,932)</th>
<th>Trisomy rare (n=11,932)</th>
<th>CNV (n=11,932)</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive</td>
<td>88</td>
<td>15</td>
<td>12</td>
<td>9</td>
<td>10</td>
<td>8</td>
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<tr>
<td>False positive</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>True Negative</td>
<td>11,843</td>
<td>11,916</td>
<td>11,919</td>
<td>11,884</td>
<td>11,915</td>
<td>11,919</td>
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<tr>
<td>False Negative</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sensitivity (%) CI</td>
<td>99.99% (99.95% - 100.00%)</td>
<td>100.00% (99.95% - 100.00%)</td>
<td>100.00% (99.95% - 100.00%)</td>
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<td>100.00% (99.95% - 100.00%)</td>
<td>100.00% (99.95% - 100.00%)</td>
</tr>
<tr>
<td>PPV (%) CI</td>
<td>99.99% (99.95% - 100.00%)</td>
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<td>100.00% (99.95% - 100.00%)</td>
</tr>
<tr>
<td>nPV (%) CI</td>
<td>100.00% (99.95% - 100.00%)</td>
<td>100.00% (99.95% - 100.00%)</td>
<td>100.00% (99.95% - 100.00%)</td>
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<td>100.00% (99.95% - 100.00%)</td>
<td>100.00% (99.95% - 100.00%)</td>
</tr>
</tbody>
</table>

Performance PrenatalSafe Karyo: follow-up (December 2016)

PPV: Positive Predictive Value; nPV: Negative Predictive Value; SCA: Sex Chromosomes Aneuploidy; CNV: Copy Number Variation.

Performance data updated from:
Fiorentino et al. The importance of determining the limit of detection of non-invasive prenatal testing methods. Prenat Diagn. 2016 Apr;36:304-11

HIGHLY RELIABLE, EXTENSIVELY VALIDATED

GENOMA Group has a history of responsible innovation, with each new advancement in NIPT characterised by reliable results and supported by extensive validation studies, published in prominent scientific journals.
This test is intended for patients at 10 weeks or greater of gestation who meet any of the following criteria:

- Maternal age-related risks (≥35 years)
- Positive results on maternal serum screening
- Abnormal ultrasound finding(s)
- Prior pregnancy with aneuploidy
- Parental translocation
- Low risk pregnancies
- Patients wanting early, accurate testing and are at average risk of aneuploidy
- Advanced paternal age (men who are >40 years old)*
- Abnormal ultrasound finding(s) suggestive of monogenic disorder*
- Patients wishing to avoid an invasive diagnostic procedure
- Patients at risk for genetic conditions screened*

* PrenatalSafe Complete test only

The test is suitable for:

- both singleton and twin pregnancies (including vanishing twin)
- pregnancies achieved by IVF techniques, including gamets donation

COMPLIMENTARY SERVICES

- Free follow-up of abnormal results
- Free CVS or Amniocentesis in collaboration with reference gynecologists
- Reimbursement of the test fee for cases with inconclusive test results
- Free RhSafe test for pregnant women Rh(D) negative with husband Rh(D) positive
- Pre- and Post-test genetic counselling
**WHY CHOOSE**

- PrenatalSafe® detects conditions that other tests can’t detect, including rare trisomies, segmental chromosomal abnormalities and monogenic disorders (inherited and de novo).
- PrenatalSafe® has the lowest false negative rate: 0% in published clinical trials.
- PrenatalSafe® differentiates between maternal and fetal DNA, which helps avoid false positives.
- Among commercially available NIPTs, PrenatalSafe® has the highest published performance.
- PrenatalSafe® is able to detect chromosomal abnormalities at low fetal fraction (<4%).
- PrenatalSafe® test offers a depth of resolution (>50 Millions reads) unlike any other noninvasive prenatal test available to date.
- PrenatalSafe® test has the lowest incidence of inconclusive results: 0.2% in published clinical trials.

**IS MORE THAN A SIMPLE TEST**

- PrenatalSafe® test is performed in an ISO 17025 accredited lab with over 20 years of experience in prenatal diagnostics, performing over 200,000 genetic tests/year.
- PrenatalSafe® test is prescribed by thousands of gynecologists worldwide.
- PrenatalSafe® test is, to date, the only NIPT that screens for both genome-wide chromosomal abnormalities and severe genetics disorders in the fetus, in a single test.
- Unlike any other NIPT available to date, PrenatalSafe® test provides complimentary confirmation of abnormal results by traditional/molecular karyotyping, and free amniocentesis or CVS.
- Unlike any other commercially available NIPT, PrenatalSafe® test provides complimentary Rh(D) testing (RhSafe).
advanced molecular diagnostics solutions using state-of-the-art technologies

Test performed in **Italy** (Rome or Milan)

**20 years** experience in prenatal molecular diagnostics

**ISO 17025 accredited laboratories** with groundbreaking Technologies

Over **200,000** genetic tests/year

**Fast TAT: from 3 working days**

**Personalised genetic counselling** with genetic counselors experts in discussing genetic test results and familial risks

Test available **worldwide**

**Dedicated R&D team**, Numerous peer-reviewed papers published in renowned international journals

---

**Next Steps**

Please call or email to find out more

**UK toll free number:** 0808 1691 022

**Email:** NIPT@Eurofins.co.uk