Over 500,000 tests performed worldwide.
Validated by a study of nearly 147,000 pregnancies.
Introduction to NIFTY®

During the last decade, developments in the science of genetics and enormous advances in genetic technologies have altered our capability to understand diseases, make diagnoses and provide effective treatments. Transforming the world of prenatal testing, the advent of new DNA-based non-invasive prenatal testing (NIPT) has introduced a highly accurate screening strategy for fetal aneuploidy.

The NIFTY® test (Non-Invasive Fetal TrisomY test) was the first NIPT to enter clinical testing in 2010 and was launched in Europe in the first quarter of 2013. Providing screening for the most common trisomies present at birth, as well as testing options for gender, sex chromosomal aneuploidies and chromosomal deletions, NIFTY® provides a significantly stronger risk indication than traditional screening procedures.

As of 2015, over 500,000 NIFTY® tests have been performed worldwide. The NIFTY® test is brought to you by BGI.

Timeline

Genetic Technology Development
Genetics Related Discovery
NIFTY® News

1866
Down syndrome discovered

1879
Discovery of chromosomes

1928
Discovery that chromosomes carry genes

1947
Discovery of circulating DNA in peripheral blood

1953
Discovery of the double helix structure of DNA

1959
Discovery of T21 as cause of Down syndrome

2005
Introduction of next generation sequencing technologies

2008
First use of NIFTY® methodology

2007
Discovery of fetal DNA circulating in maternal blood stream

2010
The first to start NIPT clinical testing

2011
First automatic sequencer

2012
NIFTY® testing for deletions added

2013
Quantity of NIFTY® samples passes 10,000

2014
NIFTY® receives approval from China FDA

Quantity of NIFTY® samples passes 400,000

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Why Non-Invasive Prenatal Testing?

Many prenatal screening options already exist. However, compared to non-invasive prenatal testing (NIPT), traditional screening methods suffer from lower accuracy and higher false positive rates. Invasive diagnostic tests such as amniocentesis or chorionic villus sampling (CVS) are accurate but carry a 1-2% risk of miscarriage.

How does NIFTY® compare to traditional screening methods?

A Comparison of Detection Rates

<table>
<thead>
<tr>
<th>Screening Method</th>
<th>Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integrated Screening</td>
<td>&gt;99%*</td>
</tr>
<tr>
<td>Serum Integrated Screening</td>
<td>&lt;96%</td>
</tr>
<tr>
<td>Quad Screening</td>
<td>&lt;88%</td>
</tr>
<tr>
<td>First Trimester Screening</td>
<td>&lt;81%</td>
</tr>
<tr>
<td>NIFTY®</td>
<td>&lt;80%</td>
</tr>
</tbody>
</table>

A Comparison of False Positive Rates (FPR)

<table>
<thead>
<tr>
<th>Screening Method</th>
<th>FPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integrated Screening</td>
<td>&lt;4%</td>
</tr>
<tr>
<td>Serum Integrated Screening</td>
<td>&lt;7%</td>
</tr>
<tr>
<td>Quad Screening</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>First Trimester Screening</td>
<td>&lt;9%</td>
</tr>
<tr>
<td>NIFTY®</td>
<td>0.05%*</td>
</tr>
</tbody>
</table>

*Non-Invasive Prenatal Testing For Trisomy 21, 18 and 13 – Clinical Experience from 146,958 Pregnancies, Wei Wang et al, Journal of Ultrasound in Obstetrics and Gynecology
Introduction to Genetic Conditions Tested by NIFTY®

**Trisomies**
A trisomy is a type of aneuploidy in which there are three chromosomes instead of the usual pair. Trisomy 21 (Down syndrome), Trisomy 18 (Edwards syndrome) and Trisomy 13 (Patau syndrome) are the three most commonly occurring autosomal chromosome aneuploidies in live births. These chromosomal conditions are caused by the presence of an extra copy or partial copy of chromosome 21, 18 or 13 respectively. This additional genetic material can cause dysmorphic features, congenital malformation and different degrees of intellectual disability.

**Deletion Syndromes**
Deletion syndromes are defined as a group of clinically recognisable disorders characterised by a small deletion of a chromosomal segment. The size and position of the deletion determine which clinical features are manifested and how severe they are. Clinical features of deletions can include developmental delays and intellectual disability, growth differences, behavioural problems, feeding difficulties, low muscle tone, seizures, dysmorphic features and a pattern of varying malformations.

**Sex Chromosomal Aneuploidies**
Sex chromosome aneuploidy is defined as a numeric abnormality of an X or Y chromosome, with addition or loss of an entire X or Y chromosome. Although most cases of sex chromosome aneuploidies are generally mild without intellectual disability, some have a well-established phenotype that can include physical abnormalities, learning delays and infertility.

### Incidence of Trisomy Conditions, Sex Chromosome Aneuploidies and Deletion Syndromes tested for by NIFTY®

![Incidence chart](chart.png)

- **Incidence per 100,000 births**
- **Prevalence undetermined**

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ISPD recognises that NIPT can be helpful as a screening test for women who are at high risk of Trisomy 21 with suitable genetic counselling. A positive test should be confirmed through invasive testing.

Source: ISPD (International Society of Prenatal Diagnosis)

The NSGC supports NIPT as an option for patients whose pregnancies are considered to be at an increased risk of certain chromosome abnormalities. Patients whose NIPT results are abnormal, or who have other factors suggestive of a chromosome abnormality, should receive genetic counselling and be given the option of standard confirmatory diagnostic testing.

Source: NSCG (National Society of Genetic Counselors)
Trisomy 21 (Down syndrome)
Trisomy 18 (Edwards syndrome)
Trisomy 13 (Patau syndrome)

Gender Identification
XXY (Klinefelter syndrome)
Monosomy X (Turner syndrome)
XXX (Triple-X)
XYY Karyotype

Deletion Syndromes
5p (Cri-du-Chat syndrome)
1p36
2q33.1

Test Information
Twin Pregnancy (trisomies only)
IVF Pregnancy
Egg Donor Pregnancy

Tested Samples: 500,000
Turnaround time 10 working days
Available from week 10 of pregnancy

Advantages

Largest capacity and coverage making NIFTY® price competitive against all other NIPT providers.

The only NIPT to offer testing services for deletion syndromes and sex chromosome aneuploidies at no extra cost.

Most validated NIPT on the market with a published study based on the outcomes of 112,000 pregnancies and over 500,000 NIFTY® tests carried out worldwide to date.

The first company to offer NIPT in clinical use worldwide.
Cell-Free DNA and Cell-Free Fetal DNA

Cell-free DNA fragments (cfDNA) are short fragments of DNA which can be found circulating in the blood. During pregnancy, cfDNA fragments originating from both the mother and fetus are present in maternal blood circulation. Cell-free fetal DNA (cffDNA) is present only as a minority component of the total cfDNA in maternal plasma, which poses a significant technical challenge for some NIPT detection methods.

The NIFTY® test requires taking a small maternal blood sample of 10ml. cffDNA in the maternal blood is then analysed to detect for chromosomal abnormality. If aneuploidy is present, small excesses or deficits in counts of the affected chromosome will be detected.

NIFTY® effectively resolves the difficulty in measuring the small increments in the specific chromosome DNA concentration through use of massively parallel sequencing technology (MPS). This means NIFTY® sequences millions of fragments of both fetal and maternal DNA from each sample. Using whole genome sequencing technology and four different proprietary bioinformatics analysis pipelines, the NIFTY® test is able to analyse data across the entire genome and compare chromosomes in the tested sample against optimal reference chromosomes to accurately determine the presence of genetic abnormality.

As opposed to the ‘targeted sequencing’ methods employed by some other NIPT tests, the NIFTY® methodology allows for highly accurate results irrespective of the clinical symptoms of the patient, and a broader range of testing options including for trisomy, sex chromosomal aneuploidy and deletion syndromes.

How does NIFTY® work?

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Sample Requirements

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Quantity</th>
<th>Requirements</th>
<th>Shipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>2ml</td>
<td>Stored in 1.5ml Eppendorf tubes, and sealed with 1cm wide parafilm.</td>
<td>Stored at -80 °C, shipped with dry ice within one week.</td>
</tr>
<tr>
<td>Maternal Blood</td>
<td>10ml</td>
<td>Gently invert the tube ten times immediately after blood sampling.</td>
<td>Stored and shipped between 6°~35 °C within 4 days. Keep the tubes upright during shipping.</td>
</tr>
</tbody>
</table>

The Test Workflow

1. Conduct pre-test genetic counseling and ensure patient provides informed consent for test
2. Discuss and fill in the NIFTY® Consent Form/Test Request Form with the patient
3. Conduct blood draw
4. Send scanned copies of Consent Form/Test Request Form and information sheet to BGI
5. Arrange collection of blood sample with DHL
6. Send Consent Form/Test Request Form with blood sample to BGI laboratory
7. Receive results back in 10 working days
8. Conduct post test genetic counseling and provide drug guidance advice as required

Becoming a NIFTY® provider is a quick and simple process. Please contact us at info@niftytest.com to find out more about partnership opportunities.

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To undergo the NIFTY® test, a pregnant woman should receive comprehensive information regarding non-invasive prenatal testing and non-directive advice on human genetics from a qualified health professional. The NIFTY® test is available from the 10th week of pregnancy.

The NIFTY® test is suitable for, but not limited to, pregnant woman who exhibit any of the following indications:

- Maternal age 35 years or older at delivery
- Fetal ultrasonographic findings indicating an increased risk of aneuploidy
- Requires reassurance following previous screening result
- Contraindications for invasive prenatal testing, such as placenta prevaria, risk of miscarriage, HBV infection etc.
- History of a prior pregnancy with a chromosomal abnormality
- Parental balanced robertsonian translocation with increased risk of fetal trisomy 13 or trisomy 21
Clinical Validation

Large scale validation of the NIFTY® test

The NIFTY® test has been validated by the world’s largest study on the clinical performance of NIPT to date.

Non-Invasive Prenatal Testing For Trisomy 21, 18 and 13 – Clinical Experience from 146,958 Pregnancies
Wei Wang et al, Journal of Ultrasound in Obstetrics and Gynecology

Samples were collected between Jan 2011 and Aug 2013. Study was published in the Journal of Ultrasound in Obstetrics and Gynecology.

Overall Sample Total with Known Pregnancy Outcomes 112,669

<table>
<thead>
<tr>
<th>Trisomy</th>
<th>TP</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>T21</td>
<td>720</td>
<td>99.17%</td>
<td>99.95%</td>
<td>92.19%</td>
<td>99.99%</td>
</tr>
<tr>
<td>T18</td>
<td>167</td>
<td>98.24%</td>
<td>99.95%</td>
<td>76.61%</td>
<td>100%</td>
</tr>
<tr>
<td>T13</td>
<td>22</td>
<td>100%</td>
<td>96.96%</td>
<td>32.84%</td>
<td>100%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>909</td>
<td>99.02%</td>
<td>99.86%</td>
<td>85.27%</td>
<td>99.99%</td>
</tr>
</tbody>
</table>

Samples with known clinical outcomes: 112,669 (karyotype or follow-up)

NIPT positive: 1,066
NIPT negative: 111,603

Unqualified samples: 211
Test failure: 145
Unknown clinical outcomes: 34,289

Overview

Total participants: 147,314
Total qualified samples: 146,958

Overview

99.17% 98.24% 100%

Combined False Positive Rate <0.05%

Read all the NIFTY® test’s published clinical data at www.niftytest.com/healthcare-providers/clinical-data/
SAFE
Non-invasive with no risk of miscarriage

SIMPLE
Test from a small 10ml maternal blood sample as early as week 10 of pregnancy

ACCURATE
Proven >99% sensitivity based on a study of nearly 147,000 pregnancies

TRUSTED
Over 500,000 tests carried out to date

www.niftytest.com
A 31 year-old pregnant woman had undergone traditional biochemical and ultrasonic fetal screening. The traditional screening assessed the risk of trisomy 21 to 1/510 corresponding to low risk. The woman was tested by NIFTY®, which identified her unborn child as being at a high risk of trisomy 21 (Figure 1). The presence of a third chromosome 21 was subsequently confirmed by karyotyping (Figure 2).

Figure 1. Scatter plot for the NIFTY® Test
Screening test: 1/510 (Low risk)
Sample ID: PDP10003761  Age: 31
NIFTY®: T21
Karyotyping: 47, XX, +21

Figure 2. NIFTY® result was confirmed by Karyotyping
A: Methodology


B: Clinical validation


C: Case study


D: Twins study


Brochure information from multiple sources, held on record.
BGI was founded in 1999 with the vision of using genomics to benefit mankind and has since become the largest genomic organization in the world. With a focus on research and applications in the healthcare, agriculture, conservation, and environmental fields, BGI has a proven track record of innovative, high profile research, which has generated over 1,000 publications, many in top-tier journals such as Nature and Science. The company also contributes to scientific communication by publishing the international research journal GigaScience.

BGI’s distinguished achievements have made a significant contribution to the development of genomics throughout the world. BGI’s goal is to make state-of-the-art genomics highly accessible to the global research community and clinical markets by integrating the industry’s broadest array of leading technologies, including BGI’s own Complete Genomics sequencing platform, economies of scale, and expert bioinformatics resources.

BGI also offers a wide portfolio of transformative genetic testing products across major diseases, enabling medical providers and patients worldwide to realize the promise of genomics-based diagnostics and personalized healthcare. BGI’s services and solutions are available in more than 50 countries around the world.
Information is for qualified healthcare professionals only.

Information is not meant to substitute qualified medical advice and is for reference only.

The NIFTY® test screens for the specific genetic conditions listed on the testing panel (as selected for testing by the patient). The purpose of the NIFTY® test is to identify pregnancies as more likely to be affected by one of the listed genetic conditions. If the test result returns as high risk, further confirmatory diagnostic testing should be performed for final diagnosis of any condition by a qualified healthcare professional.

Any patient treatment plans should only be recommended and provided by a qualified healthcare professional.

BGI recommends that non-directive genetic counseling and guidance always be provided to patients prior to undertaking any genetic testing and when reviewing results with the patient.

Accuracy of genetic testing may be affected by certain clinical factors. Therefore, test results should always be interpreted in the context of other clinical and family information of the patient.

Informed consent should always be obtained from the patient prior to testing.