NIFTY®

Non-Invasive Prenatal Testing

Screen for up to 96 Genetic Conditions Across the Whole Genome

Over 5 Million Tests Conducted

www.niftytest.com

BGI

Introduction to NIFTY®

For Reliable and Early Answers about Fetal Genetic Health Without the Miscarriage Risk of Invasive Procedures

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 aneuploidies.

The NIFTY® test (Non-Invasive Fetal TrisomY test) was one of the the first NIPTs to enter clinical testing in 2010 and was launched commercially in 2013. Providing screening for the most common trisomies present at birth, as well as testing options for sex chromosomal aneuploidies and certain chromosomal deletions/duplications, NIFTY® provides a significantly stronger risk indication than traditional screening procedures and serves as one of the most comprehensive NIPTs on the market.

To date, over 5,000,000 NIFTY® tests have been performed worldwide. The NIFTY® test is brought to you by BGI, one of the world's leading genomics organizations.

Validated by a Study on Over 147,000 Pregnancies

Noninvasive 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

Test Overview

Tested samples

5,000,000+

Turnaround time

<7 working days

Test from

week 10 of pregnancy

Test options

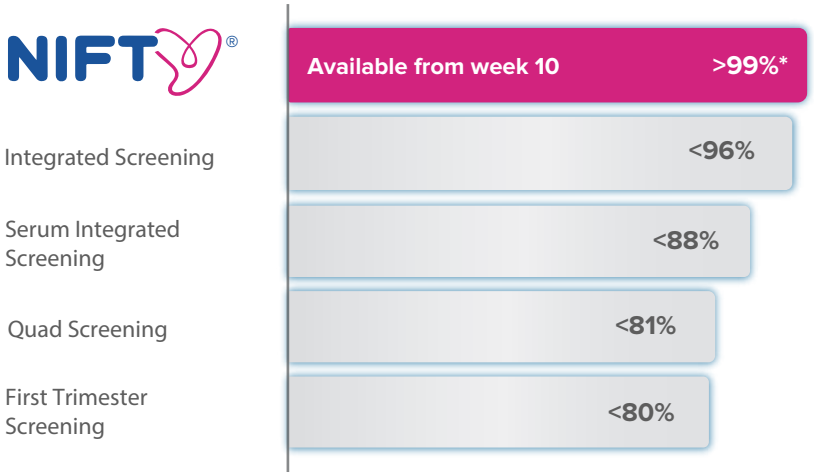
96 Genetic Conditions

- ✓ Twin Pregnancy
- ✓ IVF Pregnancy
- ✓ Egg Donor Pregnancy
- ✓ Reports cfDNA %
- ✓ Reports gender (optional)

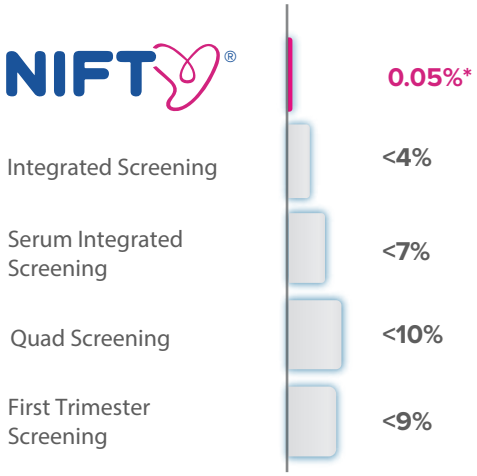
Why Non-Invasive Prenatal Testing?

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 can carry a risk of miscarriage. NIFTY® poses no risk to the mother or fetus.

Comparison of Detection Rates Between NIFTY® and Traditional Screening Tests*



Comparison of False Positive Rates (FP*R) Between NIFTY® and Traditional Screening Tests*



*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

* Accuracy figures quoted from various publicly available data sources.

NIFTY® Test Options

The NIFTY® test is one of the most comprehensive NIPTs on the market screening across all 23 pairs of chromsomes, and offers a flexible test panel with a variety of different testing options to suit partner or patient need.

Genetic Conditions

Trisomies

- Trisomy 21 (Down syndrome)
- Trisomy 18 (Edwards syndrome)
- Trisomy 13 (Patau syndrome)
- Trisomy 9
- Trisomy 16
- Trisomy 22

Sex Chromosome Aneuploidies

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

84 Deletion/Duplication Syndromes, including

- 5p (Cri-du-Chat syndrome)
- 1p36
- 2q33.1
- Prader-Willi/ Angelman Syndrome (15q11.2)
- Jacobsen Syndrome (11q23)
- DiGeorge Syndrome II (10p14-p13)
- 16p12
- Van der Woude Syndrome (1q32.2)

Why Choose NIFTY®?

The Superior Accuracy and Lower False-Positive rate of NIPT Compared to Traditional Screening Tests may Minimize Anxiety and Invasive Procedures Caused by False Positive Results*

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 for T21, 18 & 13, based on a study of nearly 147,000 pregnancies

Trusted
Over 5,000,000 NIFTY® tests carried out to date by clinicians in more than 80 countries

Comprehensive
Screening options for 96 different genetic conditions

Visit us at www.niftytest.com

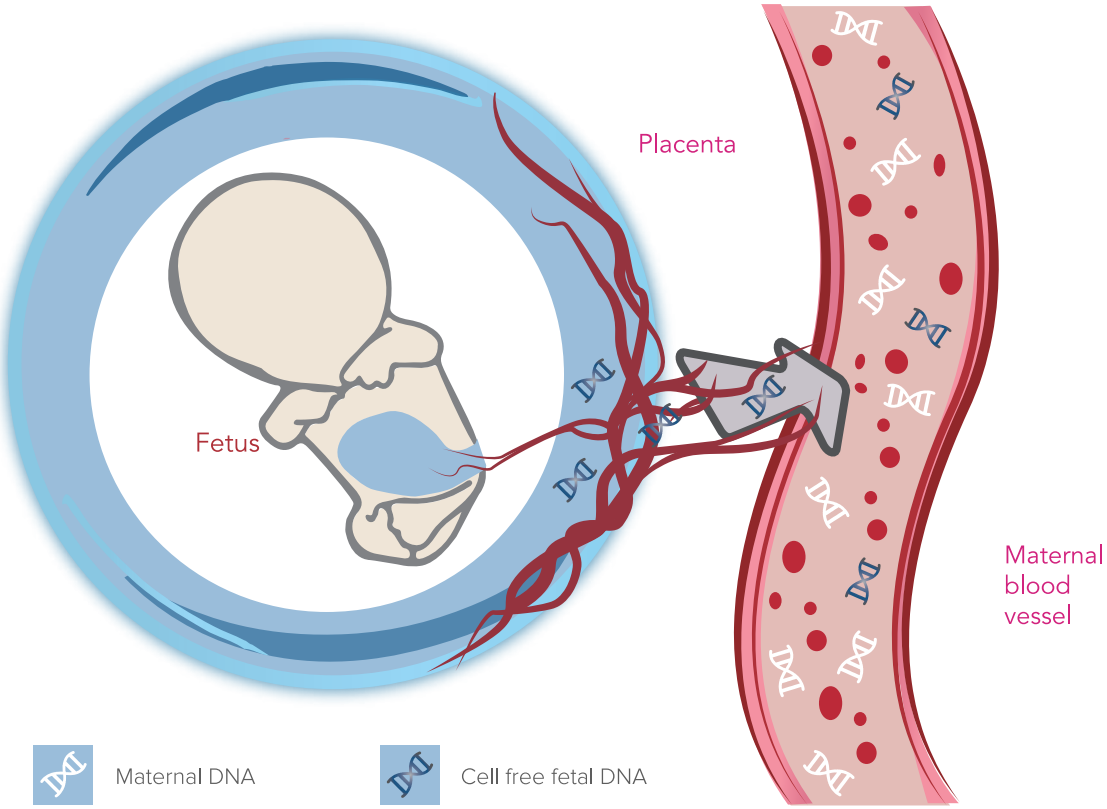
For enquiries, please email info@bgi.com

*Wax et al. J Clin Ultrasound. 2015 Jan; 43(1): 1-6

NIFTY® Methodology

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. Fetal cell-free fetal DNA (fetal cfDNA) 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.



HOW DOES NIFTY® WORK?

The NIFTY® test requires taking a small maternal blood sample of 10ml. Fetal cfDNA 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 part of the NIFTY® test's quality control procedures, the fetal cfDNA % is listed on every test report.

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 and duplication syndromes.

Introduction to Genetic Conditions Tested by NIFTY®

TRISOMIES

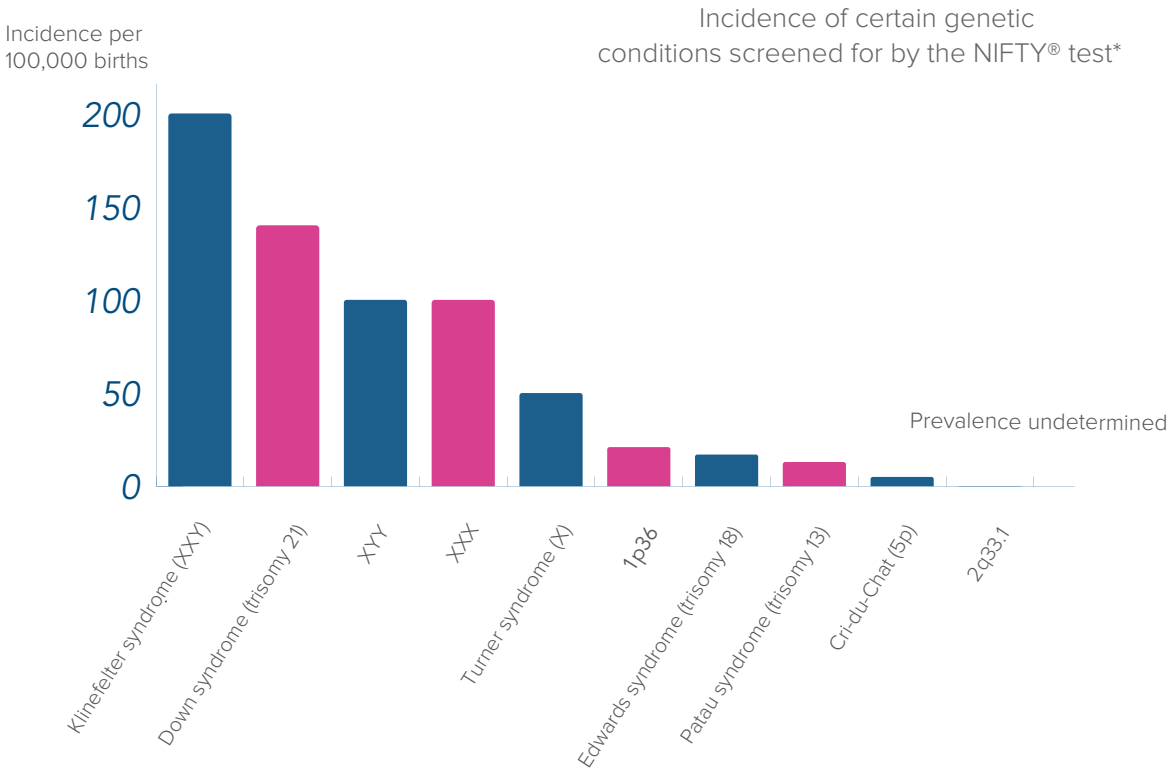
A trisomy is a type of aneuploidy in which there are three chromosomes instead of the usual pair. Trisomy 21 (Down syndrome), Trisomy 18 (Edwards syndrome) and Trisomy 13 (Patau syndrome) are the three most commonly occuring autosomal chromosome aneuploidies in live births. These chromosomal conditions 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/DUPLICATION SYNDROMES

Deletion/duplication syndromes are defined as a group of clinically recognisable disorders characterised by a small deletion or duplication of a chromosomal segment. The size and position of the deletion/duplication determine which clinical features are manifested and how severe they are. Clinical features 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.



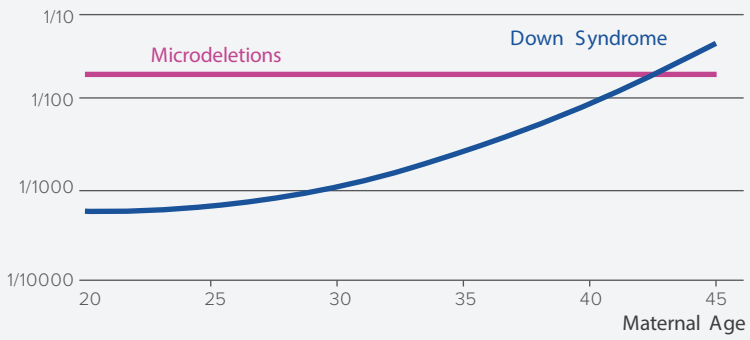
*Data taken from multiple public sources.

Microdeletion/Duplication Syndromes

Screen for 84 Different Microdeletion/Duplication Syndromes

Besides common chromosomal aneuploidies, chromosomal microdeletion/duplication syndromes (also called chromosomal copy number variations or CNVs) can also cause serious birth defects and health problems. Prevalence of these conditions ranges from 1/4000 to 1/200,000, with fragment sizes from 100K to over 10M. For pregnant women under 40 years old, the probability of being affected by microdeletions can even be higher than that of Down Syndrome.

The incidence of microdeletions can be more common than Down Syndrome for pregnant women aged under 40



Snijders,et al.ultrasound obstet gynecol 1999

ACMG
American College of Medical Genetics and Genomics

ACMG recommends that healthcare providers inform all pregnant women about the availability of NIPT screening for clinically relevant microdeletions, when counseling about the risks, benefits and limitations can be provided*

American College of Medical Genetics and Genomics (ACMG), Position Statement, Jul 2016.

Sample Requirements

Sample Type	Quantity	Requirements	Shipment
Maternal Blood	10ml	Gently invert the tube ten times immediately after blood sampling.	Stored and shipped between 6~35 ˚C within 4 days. Keep the tubes upright during shipping.

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 courier

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.

Indications

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, patients who exhibit any of the following indications:

- Maternal age 35 years or older at delivery
- Contraindications for invasive prenatal testing, such as placenta prevaria, risk of miscarriage, HBV infection etc.
- History of a prior pregnancy with a chromosomal abnormality
- Fetal ultrasonographic findings indicating an increased risk of T21, T18 or T13
- Requires reassurance following previous screening result
- Received IVF Treatment or has previosuly suffered from habitual abortion

The NIFTY® test is not suitable for patients with the following indications:

- Maternal, fetal and/or placental mosaicism (mixtures of chromosomally normal and abnormal cells in the pregnancy)
- Balanced or unbalanced translocation and chromosomal inversion
- Patients who have received a blood transfusion within one year prior to testing date
- Patients who have had transplant surgery
- Patients who have had stem cell therapy
- Vanishing twin syndrome (with developmental arrest identified has having occurred after week 8 of pregnancy and/or within 8 weeks of NIFTY® testing)

Clinical Validation

NIFTY® has been Validated by one of the World's Largest Studies on the Clinical Performance of NIPT and over 40 other Published Papers

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

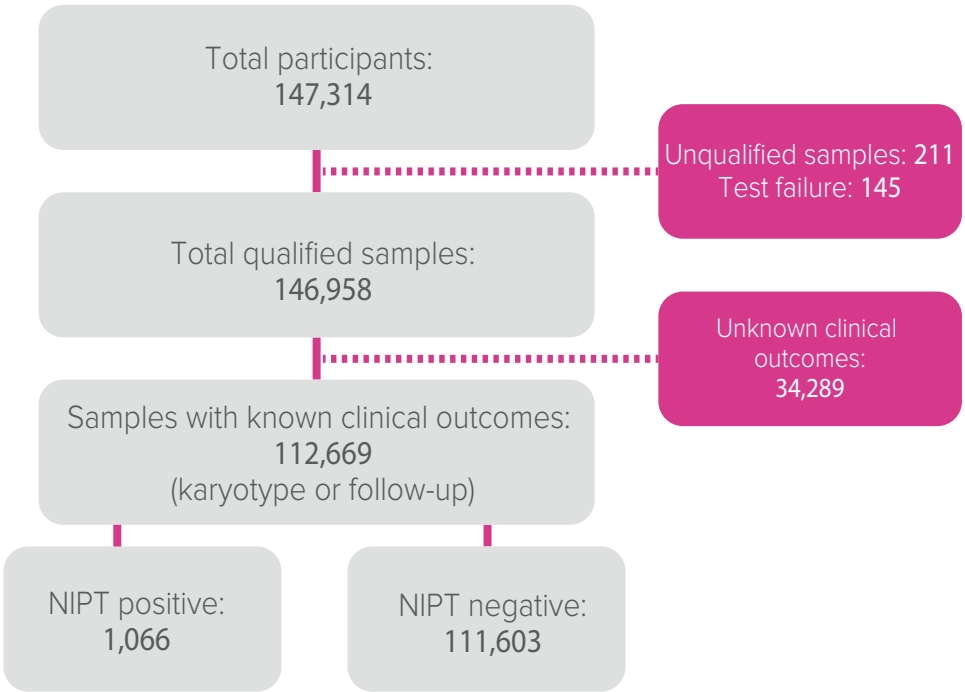
Study Population

Women aged 17-46, mean age 30.9
Gestational age at testing 9-36 weeks, mean of 18.7 weeks
Samples were collected between Jan 2011 and Aug 2013.

Study Design

147,314 NIPT requests were received from 508 medical centers for screening of fetal trisomy 21, 18, and 13 using low-coverage whole-genome sequencing of plasma cell free DNA. NIPT results were validated by karyotyping confirmation or follow-up of clinical outcomes. All participants received both pre and post test genetic counselling.

Study Overview



With the NIFTY® Test's Stringent Protocols, the High Performance of NIPT Demonstrated by Early Validation Studies can be Maintained in High Volume Clinical Services

Study Results

Overall Sample Total with Known Pregnancy Outcomes: 112,669					
Trisomy	TP	Sensitivity	Specificity	PPV	NPV
T21	720	99.17%	99.95%	92.19%	99.99%
T18	167	98.24%	99.95%	76.61%	100%
T13	22	100%	96.96%	32.84%	100%
TOTAL	909	99.02%	99.86%	85.27%	99.99%

Read all the NIFTY® test's published clinical data at www.niftytest.com/healthcare-providers/clinical-data/

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)

BGI was founded in 1999 as a nonprofit research organization to support the Human Genome Project. Over the years, BGI has grown into a multinational genomics company with significant global operations, including sequencing laboratories based in the US, Europe, Hong Kong and mainland China.

BGI 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 healthcare. BGI's services and solutions are available in more than 80 countries around the world.

www.bgi.com

NIFTY®

Contact Us:

info@bgi.com

www.niftytest.com

Follow Our Latest News:

@niftytest_

NIFTY test

Information is for qualified healthcare professionals only.

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

The NIFTY® test is not a diagnostic test. The NIFTY® test screens for the specific genetic conditions listed on the testing panel (as selected for testing). 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.

Testing availability may vary by region. The test is not for sale in the USA.