Non-Invasive Prenatal Genetic Screening

For the physician: this test information sheet should be reviewed together with the patient prior to signing the consent form.

What is NIFTY®?

NIFTY® stands for Non-Invasive Fetal TrisomY test. It is a genetic screening test pregnant woman can take from week 10 of their pregnancy. NIFTY® is a screening test, which means it **does not test with 100% accuracy**, and therefore it should not be used as the sole basis for diagnosis or other pregnancy management decisions. The NIFTY® test determines the risk of the baby having trisomy 21, trisomy 18 or trisomy 13. The term "trisomy" is used to describe the presence of an extra chromosome-or three instead of the usual pair. For example, trisomy 21 (Down syndrome) occurs when a baby is born with three copies of chromosome 21. NIFTY® also offers additional testing options for certain other rare trisomies, sex chromosome aneuploidies (an abnormal number of sex chromosomes), and copy number variations, which include deletion syndromes (a loss of part of a chromosome), duplication syndromes (an additional part of a chromosome), and certain inherited genetic disorders (a disorder caused by a gene mutation which is passed down from parent to child). Should you wish to know, the NIFTY® test can also provide gender information.

How does NIFTY® work?

During pregnancy DNA originating from the mother and the placenta circulates in the mother's blood. NIFTY® works by taking a small maternal blood sample of around 10ml and evaluating genetic information in this sample by applying whole-genome sequencing and advanced bioinformatics analysis to determine the risk of specific genetic disorders.

Test Result Information

Your test results will be sent to the healthcare provider at which you ordered the NIFTY® test. In a small minority of cases, there is not a clear result upon the first analysis. In these cases, the data must be reanalyzed and you may experience a mild delay in receiving your report. You will be notified if this happens.

"Low Risk" means there is a very low chance of the baby being affected by the conditions tested for.

"High Risk" indicates the baby has an increased chance of having one of the genetic conditions tested for. Note, NIFTY® is not a diagnostic test, a high-risk result should be followed by confirmatory diagnostic testing.

"Resample Required" – In a small number of cases, we are unfortunately unable to analyze the placental DNA in enough detail in order to provide you with a result. In these cases, we require a new blood sample in order to run a new test. There is no additional cost for resampling.

"No Call" means that we have been unable to detect a result despite resampling. The incidence of this happening is extremely low at only 0.069% of all samples received.

Test Limitations

- Although the NIFTY® test is highly accurate for identification of trisomies 21, 18 and 13, NIFTY® is NOT a diagnostic test and may result in a 'false positive' or 'false negative' result. In order to definitively confirm whether a condition exists, a diagnostic procedure, such as amniocentesis, is required. It is recommended that a HIGH-RISK result is always confirmed by a diagnostic procedure.
- Potential sources of false positive or false negative results include but are not limited to maternal, fetal and/or placental mosaicism (mixtures of chromosomally normal and abnormal cells in the pregnancy) and low fetal fraction. Blood transfusion, transplant surgery, immunotherapy and stem cell therapy can also affect test accuracy. In the case of twin pregnancy testing, 'vanishing twin syndrome' may also cause test inaccuracy. Prior to testing, you should consult with a qualified healthcare provider as to whether any of these conditions apply to you and/or advise your healthcare provider if you are already aware that any of these conditions apply to you. Test results should always be interpreted in the context of other clinical and family information.
- The result of the test does not eliminate the possibility of other abnormalities of the tested chromosomes and it does not test for other genetic disorders or birth defects.
- Abnormalities caused by chromosomal polyploid (triploid, tetraploid, etc.), chromosomal balanced translocation, inversion, ring, UPD, monogenic/polygenic disease, etc., cannot be detected by this test. This test cannot exclude the fetal mosaic chromosomal diseases.

What does NIFTY® screen for?

NIFTY®	Sensitivity Rate (singleton pregnancies)	Available for Twin Pregnancy
Trisomies ☑ Trisomy 21 (Down syndrome) ☑ Trisomy 18 (Edwards syndrome) ☑ Trisomy 13 (Patau syndrome)	>99%	Yes
Reference: Hong Y, GAO Y, Jia Z, et al. Genome-wide detection of additional fetal chromosomal abnormalities by cell-free DNA testing of 15,626 consecutive pregnant women[J]. SCIENCE CHINA Life Sciences.		

Additional Testing Options

NIFTY® pro	Sensitivity Rate (singleton pregnancies)	Available for Twin Pregnancy
Gender Identification	99.53%	Yes
Reference: Pan X, Zhang C, Li X, et al. Non-invasive fetal sex determination by maternal plasma sequencing and application in X-linked disorder counseling[J]. The Journal of Maternal-Fetal & Neonatal Medicine, 2014, 27(18): 1829-1833		
Rare Autosomal Trisomies	>99%*	No
Sex Chromosome Aneuploidies	>99%	No
References: Jiang et al. Noninvasive Fetal Trisomy (NIFTY) test: an advanced noninvasive prenatal diagnosis methodology for fetal autosomal and sex chromosomal aneuploidies. BMC Medical Genomics. 2012 5:57. Yao H, et al. Detection of fetal sex chromosome aneuploidy by massively parallel sequencing of maternal plasma DNA: initial experience in a Chinese hospital. Ultrasound Obstet Gynecol. 2014 Jul;44(1):17-24. doi:10.1002/uog.13361		
Microdeletions/ Microduplications	>90%*	No
* From in-house data. Internal analysis shows a detection rate of over 90% when cffDNA over 9.5% in selected del/dup syndromes with abnormal size over 3M.		

Before undertaking any non-invasive prenatal testing and thereafter, you should consult with a qualified healthcare professional regarding any risks, diagnoses, treatment and/or any other potentially relevant healthcare issues. A healthcare professional can supply more information about the conditions being tested for, and whether you should consider testing. You should never make decisions regarding your pregnancy without prior consultation with a qualified healthcare professional who is aware of the healthcare regulations relevant to your country of residence. BGI does not administer NIFTY® tests directly. Rather, NIFTY® tests are administered by BGI's local partners. In the event that you have not already engaged a NIFTY® partner, please contact BGI at info@bgi.com to find your nearest available test provider.

For the physician/ordering healthcare provider:
It is mandatory to ensure that a patient/guardian has signed his or her consent for the consent to conduct genetic analysis and declaration of test consent forms. BGI needs confirmation that it has been signed to be legally able to conduct genetic analysis. Please ensure that these forms are signed and that you confirm their completion on the NIFTY® test request form. You should not send these forms to BGI but you should retain copies for your records.

Your physician has recommended for you (or a person for whom you have custody and are caring for) a genetic analysis to clarify the following conditions:

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(to be completed by physician)

We would like to explain the purpose of this analysis, which occurs with a genetic test and the importance the results could have for you and your family.

The purpose of a genetic test is to study the inherited substance (DNA) using a molecular-genetic analysis of characteristics, which may be the cause of the disease that has occurred or is suspected in you or your family.

The study material is a blood sample. Normally there are no health risks when taking a blood sample. Sometimes blood can bruise (hematoma) at the drawing site or very rarely there could be nerve damage. Another risk that cannot be fully excluded exists in the extremely unlikely possibility of the samples being swapped. Every effort is made to avoid this and other mistakes.

In a genetic analysis
• either individual genetic characteristics for a specific suspicion or
• many genetic characteristics are investigated at the same time using an overview method (e.g. using exome or genome sequencing).

Importance of the results
All results will be discussed with you by your healthcare provider. It is important to note, however, that a comprehensive explanation of all possible causes of diseases due to genetic reasons is not possible. It is also not possible to exclude every disease risk for yourself and your family members (especially your children) utilizing genetic analysis.

In principle, results can occur for all testing techniques that are not directly related to the actual issue but may still be of medical importance for you and your family (so-called incidental findings). In particular, for the overview methods such as genome sequencing, incidental results can occur that relate to higher risks (that you may not be aware of) for potentially serious, unavoidable or non-treatable diseases. As part of the consent, you can decide whether and under what circumstances you wish to be informed about such incidental findings.

Right of revocation
You can withdraw your consent to the analysis at any time in full or in part without stating reasons. You have the right not to be informed about test results (right not to know), to stop the testing processes that have been started at any time up to being given the results and to request the destruction of all test material and all results collected up to that time.

Signature of Patient	Signature of Guardian (*If the patient is under 16 years old, or lacks the ability to give informed consent, guardian signature is required*)	Signature of Clinician/Healthcare Provider
_____ Day Month Year	_____ Day Month Year	_____ Day Month Year

I have read or had explained to me the attached test information sheet for the genetic screening test I am taking. I have received, read and understood a written explanation of genetic analysis. I have received appropriate explanations with regard to the disease(s) being tested for, the genetic basis, possibilities of prevention/treatment and the purpose, scope and significance of the planned genetic test(s), including the risks associated with blood sampling and the limitations of the test. I understand that this test is not intended to provide a final diagnosis and should, in case of a positive result, not be relied on as sole evidence for a diagnostic conclusion. All my questions have been answered and I have had the necessary consideration time.

I hereby confirm that I have carefully read BGI PRIVACY POLICY (available on the website http://www.bgi.com/global/), considered as part of this consent, and that I am fully aware of my rights under this policy.

I agree to provide accurate information about all previous tests such as ultrasound/other screening/diagnostic tests performed in this pregnancy. I understand that my physician may contact me for such information.

I consent to have my test results sent to the undersigned healthcare provider, or their place of business, to an address provided by them. Due to the complexity of DNA-based testing and the important implications of the test results, I understand my results will be reported through my healthcare provider and that I should contact my healthcare provider to obtain the results of the test.

I understand that my sample may be sent abroad for analysis at a BGI owned and operated laboratory (Hong Kong, China) or a BGI authorized laboratory (Thailand).

There is a possibility for the recognition of incidental findings that are not necessarily related to the reason for ordering the test. These findings can provide information that was not anticipated and that are unrelated to the individual's reported clinical features, but can be of medical value for patient care.
I choose to receive also information regarding genetic results that are not necessarily related to the specific reason for which my healthcare provider ordered the test.

□Yes **□No** **(If both are left blank, the test will not be conducted)**

-With my signature, I give my consent for genetic analysis and the necessary blood sampling. It has been pointed out to me that I can withdraw my consent in full or in part at any time without stating reasons, without any resulting detriment and that I have the right to not learn about the test results (right not to know).

-I am aware that I can stop the test once started at any time and can request the destruction of the test material including all components obtained and all result conclusions collected.

Signature of Patient

Signature of Guardian
(*If the patient is under 16 years old, or lacks the ability to give informed consent, guardian signature is required*)

Signature of Clinician/Healthcare Provider

Day Month Year

Day Month Year

Day Month Year