# PATIENT TEST INFORMATION

## Non-Invasive Prenatal Genetic Screening

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

## What is NIFTY®?

NIFTY® stands for Non-Invasive Fetal TrisomY test. It is a genetic screening test pregnant women can take from week 10 of their pregnancy. 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 for certain sex chromosome aneuploidies (an abnormal number of sex chromosomes), and deletion and duplication syndromes (a loss or addition of part of a chromosome). We offer this additional screening on an opt in basis at no extra cost (see details below). Should you wish to know, the NIFTY® test can also provide gender information

## How does NIFTY® work?

During pregnancy DNA originating from the baby circulates in the mother's blood. NIFTY® works by taking a small blood sample of around 10ml from the mother and comparing the total maternal and fetal DNA in this sample to a control sample using advanced bioinformatics analysis. The test poses no risk to the mother or baby.

## Test Result Information

Your test results will be sent to the healthcare provider at which you ordered the NIFTY® test typically within 10 working days. In around 2.5% of samples received there is inadequate concentration of fetal DNA in the blood sample. In these cases, your sample must be reanalyzed and you may experience a mild delay in receiving your report.

**"Low Risk** "means there is a very low chance of the baby having an abnormal number of chromosomes for the conditions tested for. For singleton pregnancies the risk score will be listed on the NIFTY ® report provided to you. For twin pregnancies a general risk assessment will be given.

**"High Risk"** indicates the baby has an increased chance of having one of the genetic conditions tested for. For singleton pregnancies the risk score will be listed on the NIFTY® report provided to you. For twin pregnancies a general risk assessment will be given. 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 (around 2.8%** of all samples received) we are unfortunately unable to analyze the fetal 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. In such cases, a refund of the NIFTY® test will be issued.

## Test Information

-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. In some cases, follow up confirmatory testing based on these test results could uncover maternal chromosomal or genetic conditions.

-Limited number of aneuploidy twin, egg donor and IVF pregnancies have been evaluated because these conditions are rare.

-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), balanced or unbalanced translocation, chromosomal inversion or other chromosomal abnormality in either parent, maternal metastatic cancer, and low fetal fraction. Gender identification can be false if the detected value is within the gray zone. Patients who have received a blood transfusion within one year prior to testing date, transplant surgery or stem cell therapy as well as heparin therapy, are not eligible for the NIFTY® test. NIFTY® is also unable to accept samples in cases of 'vanishing twin syndrome' where developmental arrest has been identified as occurring after week 8 of pregnancy, or within 8 weeks prior to NIFTY® testing date.

-It is strongly advised that the NIFTY® test is performed from 10 to 24 gestational weeks of pregnancy. Testing may be carried out after 24 gestational weeks only in accordance with local law. **BGI accepts no legal responsibility for testing that is provided by local healthcare partners that contravenes local law governing the provision of prenatal testing and/or prenatal healthcare.**

-Prior to testing, you should consult with a qualified healthcare provider as to whether any of the above listed conditions apply to you and/or advise your healthcare provider if you are already aware that any of the above listed 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.

**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@niftytest.com to find your nearest available test provider.**

www.niftytest.com

## What does NIFTY® screen for?

| NIFTY™ | Sensitivity Rate | Available for Twin Pregnancy |
|---|---|---|
| **Trisomies** | | |
| Trisomy 21 (Down syndrome) | 99.12% | Yes |
| Trisomy 18 (Edwards syndrome) | | Yes |
| Trisomy 13 (Patau syndrome) | | Yes |
| **Additional TestingOptions** | | |
| Gender Identification | 98%** | No |
| Trisomies | Sensitivity rate not yet validated | |
| Trisomy 9 | | No |
| Trisomy 16 | | No |
| Trisomy 12 | | No |
| **Sex Chromosome Aneuploidies** | | |
| Monosomy X (Turner syndrome) | 95% | No |
| XXY (Klinefelter syndrome) | | No |
| XXX | | No |
| XXY | | No |
| X-M | | No |
| **Deletion/Duplications** 63 types in total, see appendix below | Sensitivity rate not yet validated | No |

*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

**Figure quoted based off internal data of total samples processed worldwide (around 450,000), end of 2014.

**APPENDIX for list of Deletion Syndrome**

| | |
|---|---|
| 11q11-q13.3 duplication Syndrome | distal arthrogryposis 2B type(DA2B) |
| 12q14 microdeletion Syndrome | Smith-Magenis Syndrome |
| 14q11-q22 deletion Syndrome | Holoprosencephaly 4 type(HPE4) |
| 15q26 overgrowth Syndrome | Feingold Syndrome |
| 16p11.2-p12.2 microdeletion Syndrome | Diaphragmatic hernia, congenital (HCD/DIH1) |
| 16p11.2-p12.2 microduplication Syndrome | Dyggve-Melchior-Clausen Syndrome(DMC) |
| 17q21.31 deletion Syndrome | Holoprosencephaly 6 type(HPE6) |
| 17q21.31 duplication Syndrome | Jacobsen Syndrome |
| 1p36 microdeletion Syndrome | Langer-Giedion Syndrome(LGS) |
| 1q21.2 deletion Syndrome | Prader-Willi-like Syndrome |
| 1q21.2 duplication Syndrome | Rieger Syndrome1 type (RIEG1) |
| Wilms tumor 1 (WT1) | Van der Woude Syndrome (VWS) |
| 2q33.1 deletion Syndrome | Cat-eye Syndrome(CES) |
| 5q21.1-q31.2 deletion Syndrome | Monosomy 9p Syndrome |
| 8p23.1 deletion Syndrome | Orofaciodigital Syndrome |
| 8p23.1 duplication Syndrome | Panhypopituitarism, X-linked |
| Alpha Thalassemia, Mental Retardation Syndrome | Potocki-Lupski Syndrome (17p11.2 duplication Syndrome) |
| Androgen insensitivity Syndrome(AIS) | Leukodystrophy with 11q14.2-q14.3 |
| AngelmanSyndrome/Prader-Willi Syndrome | Mental retardation X-linked growth horm. Def (MRGH) |
| Aniridia II & WAGR Syndrome | Saethre-Chotzen Syndrome(SCS) |
| Bannayan-Riley-Ruvalcaba Syndrome(BRRS) | Sensorineural deafness and male infertility |
| Branchlootorenal dysplasiaSyndrome(BOR)/Melnick-Frazer Syndrome | Duchenne muscular dystrophy (DMD);Duchenne/Becker mascular dystrophy (DMD/BMD) |
| Microphthalmia Syndrome6 type, pituitary hypoplasia | Split-Hand/Foot Malformation 5 type (SHFM5) |
| Chromosome 10q deletion Syndrome | Split-hand/foot malformation-3 type(SHFM3) |
| Chromosome 10q22.3-q23.31 microdeletion Syndrome | Trichorhinophalangeal Syndrome1 type(TRPS1) |
| Chromosome 18p deletion Syndrome | Trichorhinophalangeal Syndrome I type |
| Chromosome 18q deletion Syndrome | Microphthalmia with linear skin defects |
| Cornelia de Lange Syndrome(CDLS) | 1q41-q42 microdeletion Syndrome |
| Cowden Syndrome(CD) | Cri du Chat(5p deletion)Syndrome |
| X-linked lymphoproliferative Syndrome(XLP) | Xp11.22-p11.23 microduplication Syndrome |
| Dandy-Walker Syndrome(DWS) | DiGeorge Syndrome2 type (DGS2) |
| | Holoprosencephaly 1 type (HPE1) |

For the physician/referring clinic: please fill in clearly using black pen and capital letters. Please ensure that a signed test request form accompanies the sample(s). Please retain a copy for your records. Please ensure the declaration of consent is reviewed and signed by the patient.

# Test Request Form

BGI Barcode

**Non-invasive Prenatal Genetic Screening**

Patient Identification Information (Eg ID ref number)

## Clinical Information

**Clinical Name**

**Ordering Clinician**

**State/Province/Country**

**Street Address**

**Zip/Postal/ Code**

**Contact Number**

**City/Country**

**Email**

Test results will be sent to this address

## Current Pregnancy

**IVF** YES□ NO□

**Date of ultrasound scan**(dd/mm/yyyy)

**Number of fetus** 1□ 2□

**Chronicity (twin)** DCDA□ MCDA□ MCMA□

**Prior Screening Test** YES□ NO□

T21 risk 1/

T18 risk 1/

T13 risk 1/

**Type of test** Combined 1st trim□ US 1st trim only□ Biochemistry 1st trim only□ 2nd trim□ Integrated test□ No test□

## Test Information

**Date of Blood Sampling**(dd/mm/yyyy)

**Gestational Age at sampling** _____weeks _____days

## Pregnancy History

**Date of last specification**

**was the baby born with health issue?** YES□ NO□

**If yes, please specify**

**Whether either parent of fetus(es) have chromosomal genetic disease** YES□ NO□

**If yes, please specify what the genetic condition is**

**,and relation with the patient** Self□ Spouse□

## Patient Information

**weight** ____ **kg** **Height** ____ **cm**

**Date of Birth (dd/mm/yyyy)**

## Test Service Information

NIFTY®

**Additional test options required (singleton pregnancies only)**

□Sex Chromosome Aneuploidies (SCA)

□Trisomies 9, 16, 22

□Trisomies 9, 16, 22+SCA

□Trisomies 9, 16, 22+SCA+Deletion/Duplication Syndromes

□Trisomies 9, 16, 22+SCA+Deletion/Duplication Syndromes +Incidental findings*

□Gender Identification+SCA

□Gender Identification+ Trisomies 9, 16, 22

□Gender Identification+ Trisomies 9, 16, 22+SCA

□Gender Identification+ Trisomies 9, 16, 22+SCA+ Deletion/Duplication Syndromes

□Gender Identification+ Trisomies 9, 16, 22+SCA+ Deletion/Duplication Syndromes+ Incidental findings*

□**Gender Identification (for both singleton and twins)**

*Patient must also consent to reporting of incidental findings on the "Patient Declaration of Consent" (see page 4)

Results will be reported for additional test options only if selected for screening here.

## Physician Statement

We/I confirm that the patient has been duly informed about the specific purpose of this genetic screening test, its risks, and its limitations.
We/I confirm that the patient has been informed that the test will cover the disorder(s) indicated on this form, and we/I will ensure that the test results will be interpreted to the patient in an appropriate manner, and that the patient will not receive the results without accompanying genetic counseling.
We/I have answered all the patient's questions with regard to this test.

**Name of Physician**

**Signature of Physician**

**Date** _____ **dd** _____**mm** _____**yyyy**

# Patient Consent Form For Conducting Genetic Analysis

For the physician:

It is mandatory to ensure that a patient/guardian has signed his or her consent to conduct genetic analyses before carrying out the test.

BGI needs confirmation in order to be legally able to conduct genetic analyses. Please ensure that the declaration of consent for the NIFTY® test on the reverse page is signed by **the patient**, and accompanies the sample(s) with the test request form. Please retain a copy 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 conditions listed and checked in P.2 “Test Service Information”.

We would like to explain the purpose of these analyses, what 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 analyses.

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.

## Patient Declaration Of Consent (please read this carefully)

NIFTY™

I have read or had explained to me the attached test information sheet for the genetic screening test I am taking (the NIFTY® test). I have received, read and understood a written explanation of genetic analyses. 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 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.

Test results can also be used for research and to improve the diagnosis and treatment of genetic diseases.
I consent to the storage and use of my anonymous test results in a statistical database for scientific purposes and to facilitate and improve the diagnosis of genetic changes and diseases in other patients. I understand that I will remain anonymous and unidentifiable during data analysis and that any personal information will be rendered non-personal beforehand in case BGI intends to use it for any reports or publications. I consent that the results stored in the database are being provided to physicians, scientists and researchers.

☐YES ☐No (if both boxes are left blank, consent shall be assumed)

Unused test material is important for researching biological mechanisms that may result in better understanding of diseases. Unused test material is also an important comparison material for quality assurance on genetic tests in the lab. I consent to the anonymous storage and use of my remaining test material for the purpose of quality assurance and the latest tracking of results beyond the testing time period. I consent to the anonymous storage and use of my test material to improve the diagnostics and treatment of genetic diseases.

☐YES ☐No (if both boxes are left blank, consent shall be assumed)

I understand that my sample will be sent abroad for analysis at a BGI owned and operated laboratory located in Hong Kong, China. And I know that there is a possibility that my sample would have been expired before arriving at BGI lab; I know that BGI is not responsible for sample expiration before arriving, and I will take expiration processing as recommended.

☐YES ☐No (if both boxes are left blank, consent shall be assumed and sample will be processed; if No, resampling will be taken)

Besides conditions listed in the chart of page one, some other chromosomal aneuploidies could be detected incidentally during the test, which will be shown in the incidental findings if you chose “Gender Identification+ Trisomies 9, 16, 22+SCA+ Deletion/Duplication Syndromes+ Incidental findings” on page 2; I know that the performance of those findings can be declined due to the limited database and reference, so the risk of false positive/negative result can be increased, and I still want to choose this option.

☐YES ☐No (if both boxes are left blank, consent shall be assumed)

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 boxes are left blank, consent shall be assumed)

*With my signature I give my consent for BGI to conduct genetic analysis of my blood sample. It has been pointed out to me that my test will not be conducted if there is a “No” chosen in the boxes above and that I can withdraw my consent in full or in part at any time without stating reasons and that I have the right to not learn about the test results (right not to know). I am aware that I can request the destruction of non-anonymous test material including all components obtained and all result conclusions collected up to that time. I am aware that anonymized reports and sample material cannot be destroyed upon my request after the anonymization. In so far I agree that with the anonymization, any title to reports and material is vested in BGI.*
*I understand that the commercial terms and conditions of sale of the test I am taking are provided by the local test provider and not BGI. I have also been noticed all the disclaimers, sample requirements and potential risk stated in the sample collection manual.*

**Signature of Patient** _____ _____ dd _____mm _____yyyy