Neuberg DIAGNOSTICS | CENTER FOR GENOMIC MEDICINE

TEST REQUISITION FORM

CHROME NON-INVASIVE PRENATAL TESTING

The most preferred non-invasive prenatal test

CHROME - NIPT evaluation and interpretation is available in the following modules:

- ☐ **CHROME - FOCUS:** analysis and reporting limited to aneuploidies involving 5 common Chromosomes: 21, 18, 13, X and Y.
- ☐ **CHROME - COMPREHENSIVE*:** analysis and reporting of aneuploidies in all 23 Chromosomes
- ☐ **CHROME - PLUS*:** analysis and reporting of aneuploidies in all 23 Chromosomes + 6 common Microdeletion Syndromes- DiGeorge (22q11.2), Angelman (15q11.2), Prader-willi (15q11.2), Cri-du-chat(5p), Wolf-Hirschhorn syndrome (4p), 1p36 deletion

PATIENT DETAILS

(In BLOCK letters)

Full Name

DOB (D D / M M / Y Y Y Y) Age (Y Y / M M) Gender ☐ M ☐ F Ethnicity

E-mail ID Contact No.

Address

Height Weight Blood Type LMP / EDC Date (D D / M M / Y Y Y Y)

Gestation Age : As per LMP ☐☐ wks ☐☐ days. As per USG ☐☐ wks ☐☐ days

Reason for referral : (Please mention details wherever available)

☐ Abnormal Biochemical Screening ☐ Abnormal Ultrasound Screening ☐ Advanced Maternal Age

☐ Twins ☐ Screening Purpose ☐ Others - .....

Pregnancy type: ☐ Singleton ☐ Multiple #(If multiple, mention number of fetuses) ☐☐

Undergone IVF: ☐ Yes ☐ No Donor Gamete: ☐ Yes ☐ No Undergone fetal reduction: ☐ Yes ☐ No

Vanishing twin*: ☐ Yes ☐ No

(#Validated only for singleton and twin pregnancies)

(*If yes, it is recommended that mother's blood be collected after 8 weeks of the event. In such cases, there is significant risk of false positive test results)

Past Obstetric History:

☐ Recurrent Pregnancy Loss ☐ Still Birth ☐ Abortion ☐ IUFD ☐ Other.....

Known parental chromosomal abnormality: ☐ Yes ☐ No

Known family or personal history of Genetic Disorders or Cancer: ☐ Yes ☐ No

Please mention details / attach report .....

CLINICIAN INFORMATION

Doctor's Name

Hospital Name

E-mail ID Contact No.

DD/MM/YYYY _____ Doctor's Signature _____

***As per PC-PNDT Act 2003, this test does not reveal the gender of the fetus.**

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TEST DETAILS

What is NIPT?

Chrome NIPT is a screening test that analyses cell-free fetal DNA for fetal aneuploidies from maternal blood. The test is performed on a maternal blood sample (approx 10 ml) which contains both maternal as well as fetal DNA (genetic material). The cell-free fetal DNA comes from the placenta, which is identical to the DNA found in the cells of the fetus in ~98% of all pregnancies. The technology used for this assay is next-generation sequencing (NGS). The Chrome NIPT has been validated for singleton, twin, and donor oocyte pregnancies.

As Chrome NIPT is a screening test, decisions about pregnancy should never be based on these screening results alone, as they neither confirm nor rule out the presence of chromosomal abnormalities in the fetus.
ACOG guidelines for screening of fetal chromosomal abnormalities recommend screening only for common chromosomal aneuploidies (Trisomy 13, 18, 21 and sex chromosomal aneuploidies).
In accordance with PCPNDT act, fetal gender is not disclosed in any of the above modules.

Who can opt for NIPT?[1]

- If the couple is concerned about risk of chromosomal abnormalities in the fetus
- Abnormal maternal serum screening result
- Advanced maternal age (>35 years)
- Previous child with a chromosomal abnormality which can be evaluated on Chrome NIPT

Sample acceptance and rejection criterion:

- A 10 ml maternal blood sample should be collected in a cell-free collection tube.
- Sample received in EDTA or heparin vial will not be accepted for Chrome NIPT. A repeat sample may be requested.
- The sample may be rejected in case a hemolyzed or inadequate blood sample is received. A repeat sample may be requested.
- Along with the sample, information regarding the maternal age, weight, number of fetus(es), fetal gestational age, ultrasound reports and Form G are required for accurate interpretation of the test results.

Expected test outcomes:

- Low risk result (aneuploidy not detected): Indicates that the chance of the fetus being affected with tested conditions is low. However, it does not guarantee normal fetal chromosomes or a healthy baby.
- High risk result (aneuploidy detected): It indicates that there is an increased chance of the fetus being affected with one of the chromosomal abnormalities listed but does not confirm that the fetus has that abnormality. The result should be confirmed by diagnostic prenatal testing such as chorionic villus sampling (CVS) or amniocentesis. False-positive results are known and may arise due to confined fetal/placental mosaicism, low level maternal mosaicism, or rarely due to the presence of maternal malignancies. Sex chromosomal anomalies when detected are reported. However, sex chromosomal abnormalities may not be detected in case of twin pregnancies.
- No call: In case of no call result, repeat sample may be requested at no additional charges However, invasive testing is recommended if the repeat testing fails to provide an answer. The probability of achieving results on a repeat sample is ~75%-80%[1]

"No call" result may arise due to:

- Administrative issues (sample collection, sample mixup and transportation)[7]
- Low fetal fraction[2]
- Assay failure (DNA extraction, amplification or sequencing- low sequence reads, high data noise etc.)[6]
- Multiple gestations (more than twins)[7]
- Maternal exposure to medications[3]
- Underlying maternal malignancies[4]

Turn Around Time (TAT):

After the receipt of the sample, NIPT results are expected within 7-10 working days. The laboratory usually ensures timely dispatch of reports, however certain un-anticipated delays may occur for which the laboratory should not be held liable for. Delay in TAT/ requirement for the repeat sample will be informed within 7 working days after the sample receipt.

Reasons for delay in TAT:

- Delay in sample shipment
- Laboratory assay failure or error (Please refer to the "No call" section).
- Other circumstances beyond your control; or unforeseen problems that may arise. The laboratory cannot be held liable for any of the above.
- The reports will be released to the referring clinician / referring center. Since genetic test results are confidential, reports / information regarding the results will not be released to any other individual/clinic without patient's consent.

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CONSENT / ASSENT FORM

Test Limitations:

- Chrome NIPT is not suitable for gestational age of <9 weeks
- NIPT cannot be performed if an expectant mother has recently (upto 3 months ago) received a blood transfusion, stem cell therapy, or organ transplantation.
- Although NIPT will detect chromosomal abnormalities in the majority of pregnancies, it cannot identify 100% of the pregnancies having aneuploidies in the screened chromosomes. The results of this test do not eliminate the possibility of abnormalities of other chromosomes, microdeletions, single-gene disorders, birth defects or other complications in the fetus.
- Chrome NIPT is not validated to detect copy number variations (CNVs).
- Chrome NIPT has not been validated for multiple gestations other than twins. The test results may differ in case of a vanishing twin.
- Sex chromosomal abnormalities might be missed in case of twin pregnancy.
- Biological factors that affect the test performance include, but are not limited to sample contamination or degradation, insufficient fetal DNA in maternal blood sample (low fetal fraction), other genetic variations in mother or fetus; unrecognised twin pregnancy, or fetal/placental/ maternal mosaicism (a mixture of cells with normal and abnormal chromosomes) and unbalanced translocations.
- About 1-2% of all the pregnancies have confined placental mosaicism. It is a situation in which the placenta has cells with chromosomal abnormality while the fetus has normal chromosomes or vice versa. This means that the chromosome in the fetus may not match the chromosomes in the DNA screened. This can lead to false positive or false negative results. False positive means NIPT result indicative of the fetus being at risk of chromosomal aneuploidy when it actually is not affected with the reported aneuploidy. False negative means, a test result that indicates that the fetus does not have a specific chromosomal aneuploidy when it actually is affected with an aneuploidy of screened chromosomes.[5]

Patient Consent:

- I understand that the data derived from my genetic testing may be de-identified and stored indefinitely as part of a laboratory database.
- I understand my de-identified data/ sample may be used for quality control, test development and laboratory improvement purposes which also include research, scientific presentations & publications.
- I have read and understood / have been explained the above information in the language of my understanding and permit the Neuberg Centre For Genomic Medicine to perform the recommended genetic analysis.
- I have had an opportunity to ask questions to my healthcare provider regarding this test, including the reliability of the test results, risk and the alternatives prior to giving my informed consent.

Name:	Signature:
Relationship to Expectant Mother:	Date, Time and Place:
Clinician Name & Signature:	

References:

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. Obstet Gynecol. 2020;136(4):e48-e69. doi:10.1097/AOG.0000000000004084
2. Hui, Lisa, and Diana W. Bianchi. "Fetal fraction and noninvasive prenatal testing: What clinicians need to know." Prenatal diagnosis 40.2 (2020): 155-163.
3. Kuhlmann-Capek M, Chiossi G, Singh P, et al. Effects of medication intake in early pregnancy on the fetal fraction of cell-free DNA testing. Prenat Diagn. 2019;39(5):361-368. doi:10.1002/pd.5436
4. Lenaerts L, Che H, Brison N, et al. Breast Cancer Detection and Treatment Monitoring Using a Noninvasive Prenatal Testing Platform: Utility in Pregnant and Nonpregnant Populations. Clin Chem. 2020;66(11):1414-1423. doi:10.1093/clinchem/hvaa196
5. Samura, Osamu, and Aikou Okamoto. "Causes of aberrant non-invasive prenatal testing for aneuploidy: A systematic review." Taiwanese Journal of Obstetrics and Gynecology 59.1 (2020): 16-20.
6. Yaron Y. The implications of non-invasive prenatal testing failures: a review of an under-discussed phenomenon. Prenat Diagn. 2016;36(5):391-396. doi:10.1002/pd.4804
7. Yin, L., Tang, Y., Lu, Q. et al. Application value of NIPT for uncommon fetal chromosomal abnormalities. Mol Cytogenet 13, 39 (2020). https://doi.org/10.1186/s13039-020-00508-z

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FORM-G

[See Rule 10]

FORM OF CONSENT

(For Non-invasive / invasive techniques)

I, _____age_____ yrs, wife/daughter of _____residing at (address) _____ _____, hereby state that I have been explained fully the probable side effects and after-effects of the prenatal diagnostic procedures. I wish to undergo the pre-natal diagnostic procedures in my interest, to find out the possibility and abnormality (i.e. deformity/deformity/disorder) in the child, I am carrying.

I undertake not to terminate the pregnancy if the pre-natal procedure/technique/test conducted show the absence of disease/deformity/disorder.

I understand that the sex of the fetus will not be disclosed to me.
I understand that breach of this undertaking will make me liable to penalty as prescribed in the Prenatal Diagnostic Technique (Regulation and Prevention of Misuse) Act, 1994 (57 of 1994).

Date : _____

Place : _____ Signature of Patient

I have explained the contents of the above consent form to the patient and/or her companion

(Name_____Address _____ _____Relationship_____) in a language she/they understand.

Date : _____

Place : _____ Signature of Clinician

Name, Signature & Registration No.
of Gynaecologist/Medical Geneticist / Radiologist/
Pediatrician / Director of the Clinic / Center / Laboratory

Name, Address& Registration No.
of Genetic Clinic / Institute [Seal]