Neuberg DIAGNOSTICS | CENTER FOR GENOMIC MEDICINE

TEST REQUISITION FORM

COMPREHENSIVE REPRODUCTIVE GENETIC TESTING

PATIENT DETAILS

Patient's Name: _____ **Date:** _____ **Age:** _____

Sex: ☐ Male ☐ Female ☐ Others **Blood Type** _____ **Height** _____

Weight _____ **Ethnicity** _____

E-mail ID _____ **Contact No:** _____

REFERRING CLINICIAN

Clinician Name _____

Hospital _____

E-mail ID* _____ **Contact No.** _____

SAMPLE DETAILS

Sample Collection Date _____ **Sample Collection Time** _____

Sample Type

☐ **Whole Blood :** ☐ EDTA (4 ml) ☐ Sodium Heparin (2 ml) (Stress Cytogenetics Test 6 ml) ☐ Streck Tube (10 ml)

☐ **Amniotic Fluid** (20 ml) ☐ **CVS** (10-15 ug) ☐ **Cord blood** (2 ml) ☐ **Product of conception** (10-15 ug in normal saline with 10 drops of Gentamicin)

☐ **Serum** (2 ml plain blood) ☐ **Dried Blood Spot** (Please refer below for available tests)

☐ **Extracted DNA** [1000 ng (20 ul x 50 ng)] ☐ **Semen** (4ml)

☐ **Embryo** ☐ **No. of biopsies** ☐ **Days** (Day 5 embryo biopsies are recommended)

☐ **Prenatal Sample :** Gestational age - ☐☐ wks (for fetal sample)

(Evaluation of maternal cell contamination is recommended for all prenatal molecular tests. Sample required: 4ml maternal EDTA Blood)

ART / IVF Pregnancy ☐ Yes ☐ No **No. of fetuses** ☐ **Donor Gamete:** ☐ Yes ☐ No

☐ **Please indicate here if this sample needs a stat/urgent report** (Rush charge may apply)

TEST REQUESTED

Biochemical Prenatal Screening

☐ **Double Marker** (Serum) ☐ **Quadruple Marker** (Serum)

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TEST REQUESTED

Prenatal Screening

Chrome Non-Invasive Prenatal Testing (NIPT) : (Whole blood in Streck tube) (Ultrasonography report is mandatory along with biochemical marker report if available)

- ☐ **NIPT Focus** (Analysis & reporting of aneuploidies in 5 common chromosomes (13,18, 21, X & Y))
- ☐ **NIPT Comprehensive** (Analysis and reporting of aneuploidies in all 23 Chromosomes)
- ☐ **NIPT Plus** (Analysis and reporting of aneuploidies in all 23 Chromosomes + 6 common microdeletions)

Pre-conception Genetic Testing

- ☐ **Carrier Screening** (> 2500 AR genes - NGS) ☐ Single ☐M ☐F ☐ Couple
- ☐ **Infertility Gene panel (ORION-Focus)**
- ☐ **Pre-implantation Genetic Testing** ☐ Aneuploidy (PGT-A / PGT-SR) ☐ Structural Aberrations (PGT-SR) ☐ Monogenic Disorders (PGT-M) (Pre-PGD work up is mandatory)
- ☐ **Pre-PGD Work up** (EDTA blood)
- ☐ **Y - Chromosomal Microdeletion**

Cytogenetics

- ☐ **Karyotyping** (Blood in Sodium Heparin/Amniotic Fluid/Cord blood) ☐ Single ☐M ☐F ☐ Couple
- ☐ **FISH**
  - ☐ (3 probes-13, 18, 21) (*Amniotic fluid / *CVS/ Sodium Heparin/ Cord blood)
  - ☐ (5 probes-13, 18, 21, X, Y) (*Amniotic fluid / *CVS/ Sodium Heparin/ Cord blood)
- ☐ **Microarray**
  - ☐ Prenatal (315K-Cytoscan Optima) (*Amniotic fluid / *CVS / Extracted DNA)
  - ☐ Constitutional (315K) (*POC / Extracted DNA / Whole blood in EDTA / Dried Blood spot) (Detects deletions upto 1Mb in size and duplication upto 2 Mb in size.)
  - ☐ Deepdive (750K) (*Amniotic fluid / *CVS / *POC / Extracted DNA / Whole blood in EDTA / Dried Blood spot) (Detects deletions and duplication upto 200kb in size.)
- ☐ **QF-PCR for Aneuploidy Detection**
- ☐ **Maternal Cell Contamination** (Maternal blood in EDTA) (*Recommended during prenatal testing - AF / CVS / Cord blood / POC)
- ☐ **Sperm DNA Fragmentation Study** (Semen) ☐ **Stress Cytogenetics** (Sodium Heparin Blood)

Molecular Genetics

- ☐ **Sanger sequencing** (Requested for ..... gene / ..... variant) (*Amniotic fluid / *CVS) (Copy of previous genetic test report is mandatory)
- ☐ **Next Generation Sequencing (NGS)** (Extracted DNA/ Whole Blood EDTA/ Amniotic Fluid/ CVS/ Dried Blood Spot)
  - ☐ **ORION Single gene** (Requested for ..... gene)
  - ☐ **ORION Focus** (Pre designed disease specific gene panel) *Please contact lab for gene list & panel details
  - ☐ **ORION WES** (Phenotype based Whole Exome +CNV Analysis) (Please specify Phenotype)
  - ☐ **Scale Up to ORION** (Single gene/ focus scaled to WES)
  - ☐ **ORION Plus** (Phenotype based Whole Exome + CNV Analysis + Mitochondrial Genome Sequencing)
- ☐ ***MLPA (Requested for _____ gene)** ☐ **Others (Specify _____)**

*Please contact Lab for details

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CLINICAL DIAGNOSIS

Clinical Details / Pedigree :

(Please provide detailed clinical information including age of onset of symptoms, disease progression, current status, response to treatment, presence of consanguinity, family history and relevant investigations performed.)

(Relevant documents can be emailed to contact@ncgmglobal.com)

Details of samples sent along with for additional testing

	Name	DOB / Age	Relationship (with patient)	Affected (Yes / No)	Details
1)					
2)					
3)					
4)					

I have had the opportunity to ask questions to my healthcare provider regarding this test, including the reliability of test results, the risks and the alternatives prior to giving my informed consent.

☐ **I have read and understood the above/have been explained the above in a language of my understanding and permit NCGM to perform the recommended genetic analysis.**

☐ **I understand that the data derived from my genetic testing may be stored indefinitely as a part of the laboratory database. This data is always stored in de-identified form. I understand my de-identified data/ sample may be used for research collaborations as well as scientific presentations and publications.**

Name:

Signature:

Relationship to Patient:

Date, Time and Place:

Clinician Name & Signature:

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A. Pre-conceptional testing helps you to make an informed reproductive decision. It includes different types of tests:

1. Carrier Screening {(includes NGS testing for > 2500 genes associated with > 2990 OMIM phenotypes + SMA-MLPA of the couple + DMD MLPA (female) + Fragile X Screen PCR (female)}

This test determines whether an asymptomatic individual is a carrier of an autosomal recessive or X-linked recessive disorder. It focuses only on the coding portions (exons) as well as surrounding splice sites of genes currently associated with human disease: Mendeliome. It enables you to understand whether your children are at risk of having any of the tested disorders. A positive report helps assess the risk of having an affected child and allows you access to reproductive options to prevent/manage the same. A negative/normal report reduces the likelihood of having an affected child with any of the disorders tested above but does not exclude it completely due to technical limitations of NGS technology. A negative or normal report does not exclude the risk of having children affected with chromosomal abnormalities, de novo mutations and autosomal dominant disorders. The test may not be suitable in families with an autosomal dominant disorder or disorders caused due to copy number variations. Need for further testing may arise based on the above results. This test can be performed as a combined screen on the couple or as a sequential test or in one individual as deemed necessary by your referring clinician.

2. Pre-implantation Genetic Testing-Aneuploidies (PGT-A/PGT-SR)

PGT-A and PGT-SR are the screening tests to screen embryos for chromosomal aneuploidies and structural aberrations. It assists in the process of selecting healthy embryos with normal number of chromosomes for implantation.

3. Pre-implantation Genetic Testing- Monogenic Disorders/Diagnosis (PGT-M/ PGD)

This technique is used when there is a history of genetic condition due to single gene mutations in the family. The test is possible only when a disease causing variant has been identified in the family. The technique is based on testing embryos for the relevant genetic variations. Results of this test help in selecting unaffected embryos for transfer thus reducing the risk of having an affected child. The test can only be performed on embryos after pre-requisite work up termed as Pre-PGD/Pre-PGT-A work up.

There are certain types of genetic variations which are still under validation and hence kindly contact the lab for feasibility of PGT-M.

B. Aneuploidy Screening

There is a risk in every conception that the baby may be affected with a chromosomal abnormality, most common being chromosomal aneuploidies (numerical variations).

Various modalities of screening include:

1. Biochemical tests (Double and Quadruple Marker Screening)

1st trimester double marker test measures the levels of pregnancy associated plasma protein (PAPP-A) and human chorionic gonadotropin (HCG) in the mother's blood. This is a screening test to evaluate the risk for chromosomal abnormalities like Trisomy 13, Trisomy 18, and Trisomy 21 and can be done between 11th to 13th weeks of pregnancy. When combined with the nuchal translucency scan (perfomed between 11-13+6 weeks) the first trimerster screen can detect 82-87% of affected at-risk pregnancies.

Quadruple marker test evaluates the levels of alpha fetoprotein, HCG, unconjugated oestriol, and serum inhibin-A in the mother's blood sample. It can be done between 15th to 18th weeks of pregnancy. It has a detection rate of 81%.

2. CHROME-NIPT

Non invasive prenatal testing (NIPT) determines the risk of your child being born with common chromosomal aneuploidies. It tests the baby's circulating DNA in mother's blood and can be performed as early as 9 weeks of pregnancy. The detection rate for Trisomy 21 is 99% and a negative test excludes the same by 99.9% The American College of Obstetrics and Gynecology as well as the Society of Maternal and Fetal Medicine recommend offering NIPT as a screening test to all pregnant women. As NIPT is a screening test, positive/high risk results need to be confirmed via invasive testing.

The above screening test are currently validated for detection of common chromosomal aneuploidies only. They do not detect the risk of copy number variations/ balanced re-arrangements and structural variations.

C. Prenatal Testing

Prenatal testing involves tests performed on fetal (unborn baby's) sample to determine whether the fetus (unborn baby) has a chromosomal or genetic abnormality. It is done by invasive testing as it requires a fetal sample and is associated with a risk of procedure-related pregnancy loss (0.5-1%).

The following test can be performed on the fetal sample as indicated by your referring clinician.

1. Cytogenetic Tests

(1) Karyotyping: A Karyotype pictures the chromosomes of an individual to determine the chromosome constitution and assess numerical or large structural abnormalities.

(2) FISH (Trisomy 13, 18, 21, X, Y): It helps visualize specific regions of chromosome to assess chromosomal abnormalities

(3) Chromosomal Microarray (CMA): This test evaluates individual's chromosomes in much greater detail than karyotype or FISH. It allows detection of smaller changes in the chromosomes. It however cannot detect balanced re-arrangements. The CMA - 315K detects deletions upto 1Mb in size and duplication upto 2 Mb in size. The CMA-750K detects deletions and duplication upto 200kb in size.

2. Molecular Tests

Sanger Sequencing: This test determines the nucleotide sequence of the DNA to determine change in nucleotides causing the genetic disorder. This test can be used when a family specific mutation is known to evaluate the risk in the pregnancy.

NGS: It is a high throughput massively parallel sequencing platform which enables sequencing of thousands of genes. This technique is recommended when there is a family history of a genetic disorder or in case of fetal malformations as indicated by your referring clinician. The technology is specific to certain types of genetic variations (does not include triplet repeat expansions, methylation abnormalities etc.)

Due to inherent difference in gene structure, certain genes/ portions of a gene may not be well covered. Reporting is based on the American College of Medical Genetics guidelines and current available scientific evidence and may vary as new information is available.

Bibliography

1. Sensitivity and specificity of prenatal screening methods for detection of risk of fetal chromosomal abnormalities . Sunil Kumar Juneja, Pooja Tandon, Anjali Sharma, Anshu Sharma. s.l. : International Journal of Reproduction, Contraception, Obstetrics and Gynecology , 2019, Vols. 9(2):540-544 .

2.Screening for Fetal Chromosomal Abnormalities. Practice Bulletins — Obstetrics the American College of Obstetricians and Gynecologists' Committee on. s.l. : ACOG PRACTICE BULLETIN, 2020.

3. Kagan, K. O., et al. "First trimester risk assessment based on ultrasound and cell free DNA vs combined screening: a randomized controlled trial." Ultrasound in Obstetrics & Gynecology 51.4 (2018): 437-444.

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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 Patient

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]