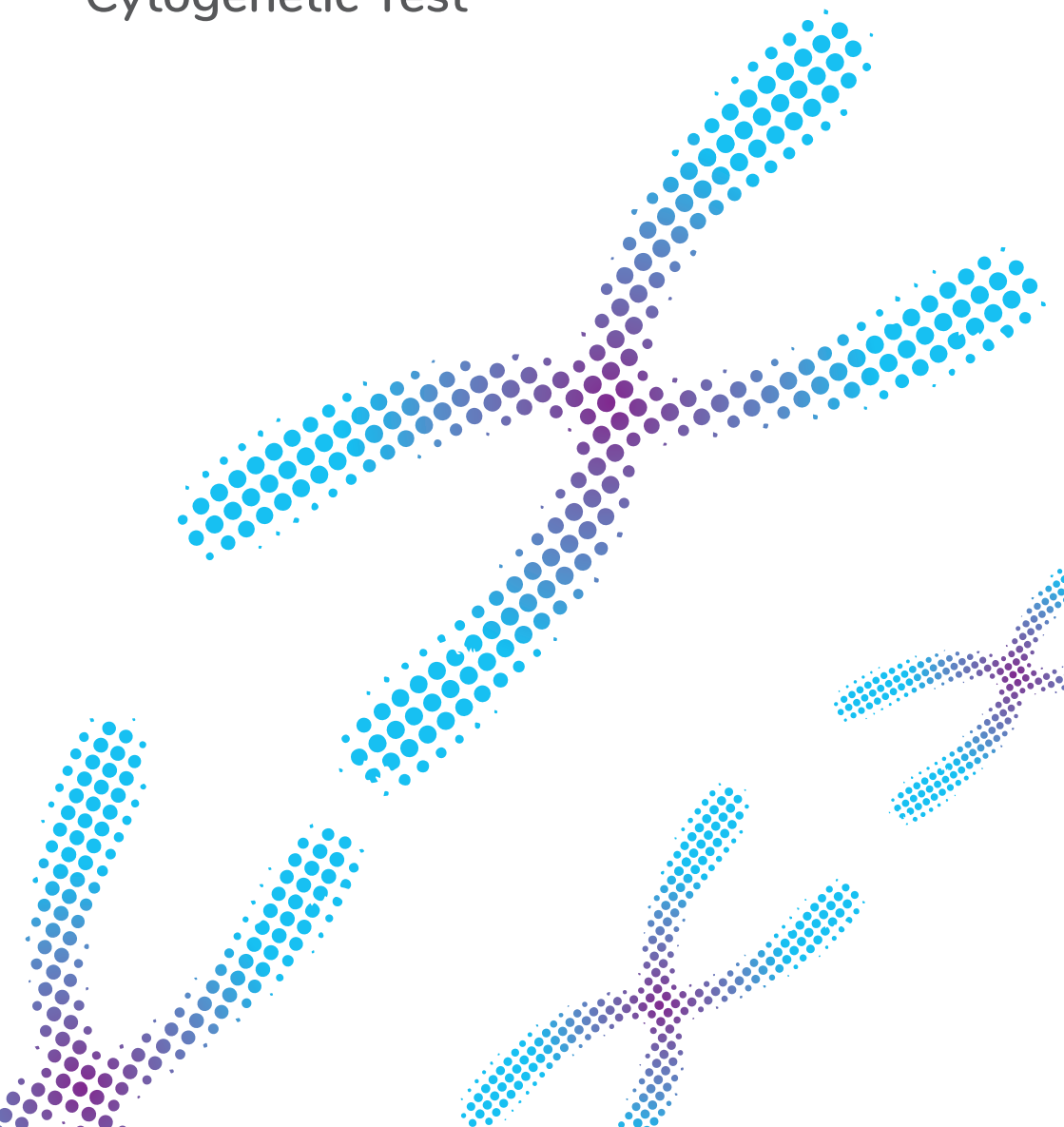
Claria
Reproductive Genetics

MEDGENOME

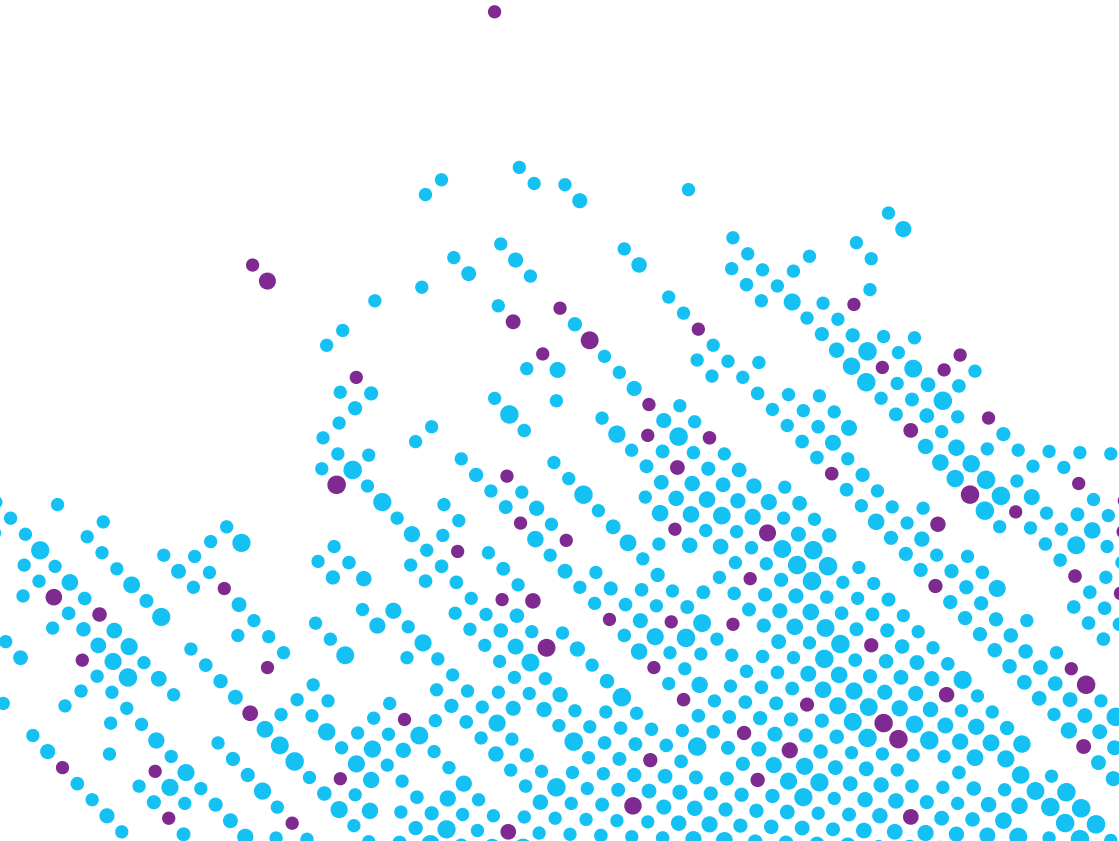
# MedGenome
# Center For Genetic Health Care

## Cytogenetic Test



## *MedGenome offers the most comprehensive range of reproductive genetic testing services*

- Non Invasive Prenatal Test
- Carrier Screening Test
- Preimplantation Genetic Screening/Diagnosis
- Products of Conception
- Karyotyping
- FISH
- Prenatal Diagnostic Services
- Genetic Counselling

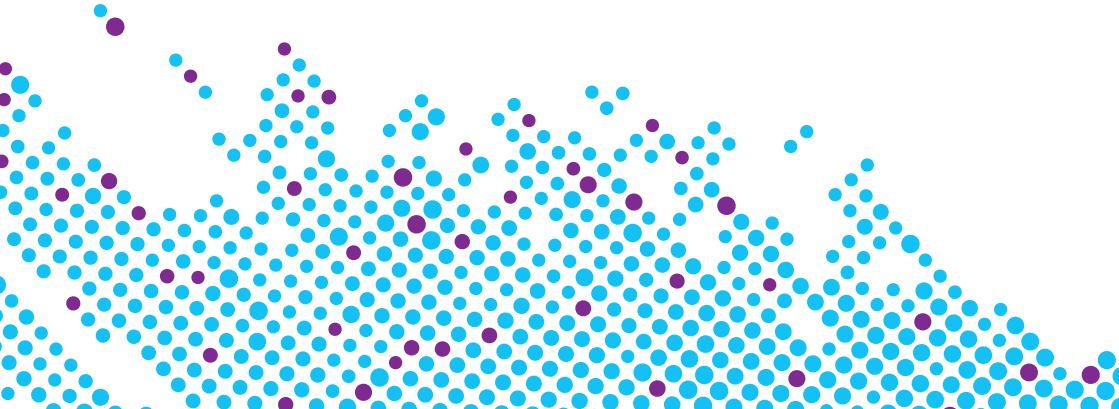


# *About MedGenome Center for Genetic Health Care*

Medical genetics plays an important role in all aspects of medical practice: prevention, screening, diagnosis and management. About 60% of pregnancy losses, 2-3% of all neonate and 50% of childhood deafness, blindness, mental retardation and 1 to 10% of all malignancies are directly due to genetic factors.

Dr. Hema Purandarey, Director of the MedGenome Center for Genetic Health Care (CGHC) is well known in the field of medical genetics. She has been trained in all aspects of medical genetics at the most advanced centers/laboratories over the world (USA, UK and Europe).

The centre has a team of physicians, trained and dedicated scientific and technical staff. The centre is also equipped with state-of-the-art equipment. The center has vast experience, receiving more than 5000 referrals per year for genetic testing.



# *Tests offered at MedGenome CGHC*

MedGenome CGHC offers a range of tests covering the broad spectrum of reproductive and prenatal cytogenetic testing services. The tests that we offer can be broadly classified into the following headings:

- Prenatal Cytogenetic Testing
- Karyotyping and High-Resolution Banding
- POC Testing by Cytogenetics
- Male Fertility Tests
- Chromosomal Microarray Testing

MedGenome also offers a wide variety of Molecular Genetic Tests in Prenatal/ Postnatal, Cancer and Medical Genetics segments.

# *Prenatal Genetic Testing-Chorionic Villus Sampling:*

Chorionic Villi are projection from the developing fetus into the placenta. Chorionic Villus Sampling (Biopsy) is usually done between 10th to 12th weeks of Gestation.
At the MedGenome Center for Genetic Health Care we offer the following Cytogenetic Tests for CVS samples:

| Test Code | Test Name | Sample | Method | TAT (Working Days) |
|---|---|---|---|---|
| MGM1105 | CVS Karyotyping only |  | Karyotyping + FISH | 10 |
| MGM1112 | CVS Karyotyping+ FISH (2 probes) (either 13/21 or 18/X/Y) | | | |
| MGM1111 | CVS Karyotyping+ FISH (5 probes 13,18,21, X/Y) | | | |
| AVAILABLE AT MUMBAI ONLY | | | | |
| MGM1126 | CVS Procedure+ Karyotyping | | | |
| MGM1127 | CVS Procedure+ Karyotyping+ FISH (2 probes) (either 13/21 or 18/X/Y) | | | |
| MGM1128 | CVS Procedure+ Karyotyping+ FISH (5 probes 13,18,21, X/Y) | | | |

For sample collection details please check page 15.

# *Prenatal Genetic Testing-Amniotic Fluid Testing:*

Amniotic fluid contains cells known as Amniocytes which can be cultured and analyzed for genetic abnormalities including Chromosomal Aneuploidies. This test is done between the 15th and 18th weeks of gestation.

At the MedGenome Center for Genetic Health Care we offer the following Cytogenetic Test on Amniotic Fluid:

| Test Code | Test Name | Sample | Method | TAT (Working Days) |
|---|---|---|---|---|
| MGM1106 | Amniotic Fluid karyotyping only |  | Karyotyping + FISH | 15 |
| MGM1113 | Amniotic Fluid karyotyping + FISH (5 probes -13,18,21, X/Y) | | | |
| MGM1114 | Amniotic Fluid Karyotyping + FISH (2 probes) (either 13/21 or18/X/Y) | | | |
| AVAILABLE AT MUMBAI ONLY | | | | |
| MGM1129 | Amniocentesis + Karyotyping | | | |
| MGM1130 | Amniocentesis + Karyotyping + FISH (5 probes:13,18,21, X/Y) | | | |
| MGM1131 | Amniocentesis+ Karyotyping + FISH (2 probes: either 13/21 or 18/X/Y) | | | |

For sample collection details please check page 15.

# *Prenatal Genetic Testing-Cordocentesis:*

This process involves collection of a few ml of blood from the umbilical cord vein. This test is usually done for anomalies detected later during the pregnancy or if the patient has come later for prenatal testing. This process is usually done on or after 18th week of pregnancy.

At the MedGenome Center for Genetic Health Care we offer the following Cytogenetic Tests for Cord Blood Samples:

| Test Code | Test Name | Sample | Method | TAT (Working Days) |
|---|---|---|---|---|
| MGM1107 | Cord Blood karyotyping only |  | Karyotyping + FISH | 8 |
| MGM1115 | Cord Blood karyotyping + FISH (5 probes -13, 18, 21, X/Y) | | | |
| MGM1116 | Cord blood karyotyping + FISH (2 probes) (either 13/21 or 18/) | | | |
| AVAILABLE AT MUMBAI ONLY | | | | |
| MGM1132 | Cord Blood Procedure + Karyotyping | | | |
| MGM1133 | Cord Blood Procedure + Karyotyping + FISH (5 probes 13, 18, 21, X/Y) | | | |
| MGM1134 | Cord Blood Procedure + Karyotyping + FISH (2 probes 13/ 18 or 21, X/Y) | | | |

For sample collection details please check page 15.

## *Microdeletion Testing by FISH (Selected):*

- Microdeletion syndromes are usually caused by deletions in the chromosome of <5 Mb in size
- These syndromes occur with different frequencies and independent of maternal age
- Microdeletions are difficult to identify using conventional Karyotyping, therefore FISH is recommended

## *Prader Willi Syndrome:*

- Caused by 5.9Mb deletion at 15q11-q13 region in the Paternal Chromosome
- Frequency of occurrence is 1 in 10,000 births
- Symptoms: Hypotonia, insatiable appetite mild to moderate mental retardation and intellectual disabilities

## *Angelman's Syndrome:*

- Caused by 5.9Mb deletion at 15q11-q13 region in the Maternal Chromosome
- Frequency of occurrence is 1 in 12,000 births
- Symptoms: Hypotonia, insatiable appetite mild to moderate mental retardation and intellectual disabilities

## *DiGeorge Syndrome:*

- Most common chromosomal abnormality after Trisomy 21 with a frequency of 1 in 2,000 live births.
- Caused by 3Mb deletion at 22q11.2 region of Chromosome 22
- Symptoms: Reduced lifespan with mild to moderate mental retardation, **cardiac anomalies, cleft lip/palate**

# *William's Syndrome:*

- This is caused by a 1.8 Mb deletion at 7q11.23 region of Chromosome 7
- Occurs with a frequency of 1 in 10,000 live births
- Symptoms: Mild to moderate intellectual disability, cardiovascular disorders including supravalvular aortic stenosis (SVAS), hypercalcemia

At the MedGenome Center for Genetic Health Care we offer the following Cytogenetic Tests:

| Test Code | Test Name | Sample | Method | TAT (Working Days) |
|---|---|---|---|---|
| MGM1103 | Prader-Willi/ Angelman |  | Karyotyping + FISH | 9 |
| MGM1104 | DiGeorge/ VCF syndrome | | | |
| MGM1063 | Williams Syndrome | | | |

For sample collection details please check page 15.

# *Karyotyping:*

- Gold standard for Cytogenetic analysis
- Cells collected from the patient are cultured and arrested at Metaphase and then the chromosomal complement of the cells is analyzed
- Used to analyze aneuploidies, chromosomal gain and losses >5Mb, balanced translocations and large chromosomal inversions
- Resolution in terms of number of bands in karyotyping is 350

# *High-Resolution Banding*

- Here cells are arrested at pro-metaphase and then karyotyping is done
- This increases the number of band from 350 up to 500-800 bands
- Higher resolution of detecting smaller deletion between 3-5Mb[1]

**At the MedGenome Center for Genetic Health Care we offer the following Karyotyping and HRB Tests:**

| Test Code | Test Name | Sample | Method | TAT (Working Days) |
|---|---|---|---|---|
| MGM575 | Karyotyping (Non-Leukemia) |  | Karyotyping + FISH | 15 |
| MGM1099 | High Resolution Banding (HRB) | | | |

For sample collection details please check page 15.

[1] Shaffer LG, Bejjani BA. A cytogeneticist's perspective on genomic microarrays. Hum. Reprod. Update. 2004 May-Jun;10(3):221-6.

# *Products of Conception (POC) Testing*

- Etiology of abortion is multifactorial (endocrine, anatomic, immunological, infectious, environmental and genetic factors)
- 50% are due to chromosomal abnormalities (numerical and structural anomalies).
- Approximately 60–70% of first-trimester miscarriages are caused by chromosomal abnormalities, including aneuploidies, triploidy, uniparental disomy (UPD)[2,3]
- The most frequent cytogenetic abnormalities are numerical aberrations (86%), mainly trisomy (75%), polyploidy (13%) and monosomy followed by structural rearrangements (6%) and other abnormalities such as chromosomal mosaicism or double and triple trisomies (8%)[4,5,6]
- Essential to test these products to help determine the underlying genetic causes for the miscarriage.

At the MedGenome Center for Genetic Health Care we offer the following POC tests:

| Test Code | Test Name | Specimen Type* | Methodology | TAT (Working days) |
|---|---|---|---|---|
| MGM1110 | POC all trimester + FISH (7probes) |  | Karyotyping + FISH* | 15 |
| MGM1100 | POC-1st trimester | | | |
| MGM1101 | POC-2nd trimester | | | |
| MGM1102 | POC-2nd and 3rd trimester cord/ cardiac blood | | | |

* FISH is only performed as a reflex test for POC samples, if cell culture fails.

For sample collection details please check page 15.

[2] Levy B., et al. Genomic imbalance in products of conception: single-nucleotide polymorphism chromosomal microarray analysis. Obstetrics and Gynecology 124(2 Pt 1):202–209 (2014).

[3] Wang B. T., et al. Abnormalities in spontaneous abortions detected by G-banding and chromosomal microarray analysis (CMA) at a national reference laboratory. Molecular Cytogenetics 7:33 (2014). eCollection 2014. doi:10.1186/1755-8166-7-33

[4] Lomax B, Tang S, Separovic E, Phillips D, Hillard E, Thomson T, Kalousek DK. Comparative genomic hybridization in combination with flow cytometry improves results of cytogenetic analysis of spontaneous abortions. Am J Hum Genet. 2000 May; 66(5):1516-21.

[5] Goddijn M, Leschot NJ Genetic aspects of miscarriage. Baillieres Best Pract Res Clin Obstet Gynaecol. 2000 Oct; 14(5):855-65.

[6] Sandra García-Herrero, Inmaculada Campos-Galindo, José Antonio Martínez-Conejero, et al., "BACs on-Beads Technology:A Reliable Test for Rapid Detection of Aneuploidies and Microdeletions in Prenatal Diagnosis," BioMed Research International, vol. 2014, Article ID 590298, 7 pages, 2014.

# *Male Fertility Testing:*

- Contributes about 40-50% of the total infertility burden. Chromosomal aberrations, either numerical or structural in nature, can have profound effects on fertility
- Chromosomal aberrations when analyzed in male presenting with infertility is 2%–14%[7]
- Essential to test for chromosomal aneuploidies, Y chromosome deletions and sperm aneuploidies
- These tests would provide a better understanding for any underlying cytogenetic changes contributing to male infertility

At the MedGenome Center for Genetic Health Care we offer the following Cytogenetic tests for Male Fertility:

| Test Code | Test Name | Specimen Type* | Methodology | TAT (Working days) |
|---|---|---|---|---|
| MGM1094 | Sperm FISH (For common aneuploidy 13, 18, 21, X and Y) |  | FISH | 4 |
| MGM1095 | Y chromosome Deletion by High Resolution Banding (HRB) |  | Karyotyping | 15 |

For sample collection details please check page 15.

[7] Shi Q, Martin RH. Aneuploidy in human sperm: a review of the frequency and distribution of aneuploidy, effects of donor age and lifestyle factors. Cytogenet Cell Genet 2000; 90: 219–26.

# *Chromosomal Microarray (CMA) Testing:*

- Offer unparalled screening for deletions, duplications, loss of heterozygosity for all chromosomes
- These microarrays can be used for a wide variety of purposes from POC analysis to the first test choice for Development Delay, Multiple Congenital Anomalies, Mental Retardation and Autism Spectrum Disorders
- Based on the number of probes available of the microarray chip; currently we offer the following microarrays for testing purposes:

| Test Code | Cytoscan Array | Probe Density | Reportable Ranges | | | | | Sample & Transport | TAT (Working days) |
|---|---|---|---|---|---|---|---|---|---|
| | | | Loss (Deletion) | Gain (Duplication) | Loss of Heterozygosity (LOH) | Absence of Heterozygosity (AOH) | Long Continuous Stretch of Homozygosity (LCSH) | | |
| MGM514 | Optima | >200Kb* | > 1 Mb | > 2 Mb | > 5 Mb | Not Reported | Not Reported |  Transport: Ambient | 14 |
| MGM294 | 750K | >100Kb | >100kb | >400kb | >5 Mb | > 3% of total autosomal (>3Mb LCSH) | LCSH >8-15 Mb | | |
| MGM295 | HD | >25Kb | >25Kb | >200Kb | >100Kb | > 3% of total autosomal (>3Mb LCSH) | LCSH >8-15 Mb | | |

*This is the probe density at specific regions of the genome.

Please note conditions for Peripheral blood and Products of Conception for CMA are different and indicated separately on Page 15.

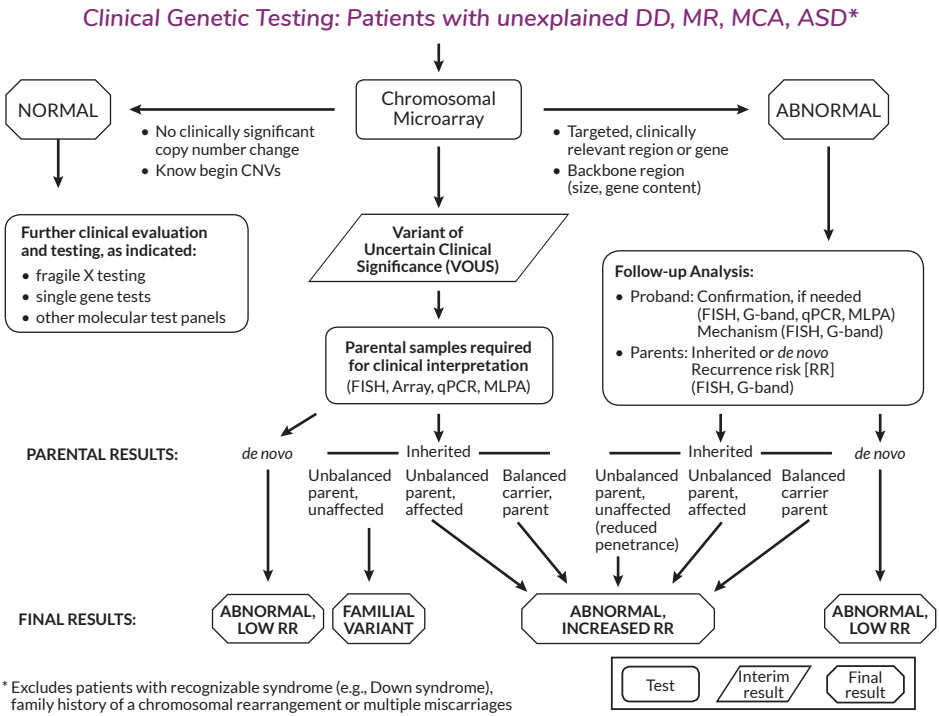



Fig. 1: International Standard Cytogenomic Array Consortium (ISCA) Guidelines for using Chromosomal Microarray in Patients with unexplained Developmental Delay (DD), Mental Retardation (MR), Multiple Congenital Anomalies (MCA) and Autism Spectrum Disorders (ASD)[8]

## Maternal Cell Contamination (MCC) Test:

- Mandatory for all prenatal samples and POC undergoing molecular genetic testing (including Chromosomal Microarray)
- Ensures that the prenatal/ POC sample is free of maternal cells/DNA which acts as a contaminant for the test
- Only samples which are negative for MCC can be reported

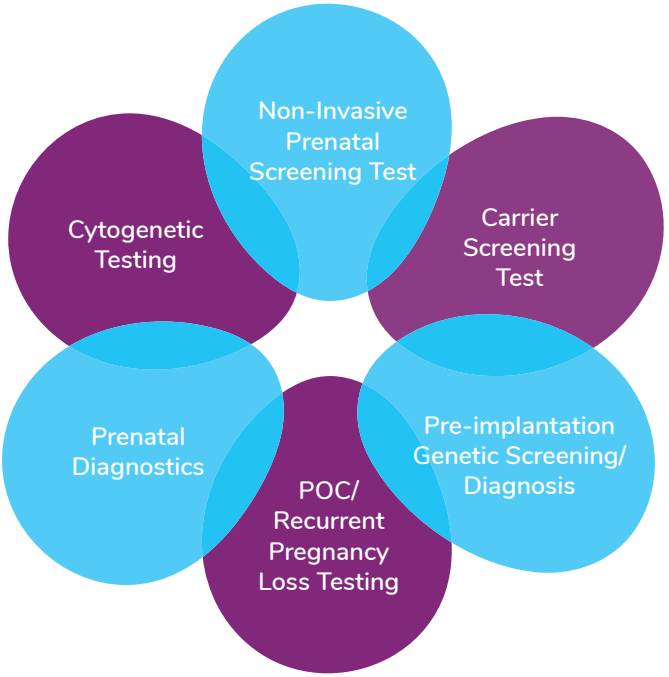
| Test Code | Test Name | Specimen Type* | Methodology | TAT (Working days) |
|---|---|---|---|---|
| MGM345 | Maternal Cell Contamination (MCC) check in prenatal DNA | Maternal peripheral blood in addition to Prenatal or POC sample | Fragment Analysis | 7 |

For sample collection details please check page 15.

| Sample | | Sample Collection | Transport Conditions | Sample Volume |
|---|---|---|---|---|
|  | Amniotic fluid | Amniotic fluid in a sterile falcon tube/cultured cell | Ambient temperature. Do not freeze | 20 ml taken in 2 sterile 15ml Falcon tubes |
|  | Chorionic villus sample (CVS) | CVS In a sterile 15ml Falcon tube with RPMI1640 + 10% FBS + 1% antibiotic | Ambient Temperature. Do not freeze | CVS 20 - 30mg in provided medium |
|  | Cord Blood | Sodium heparin-(green cap) vacutainer | Ambient Temperature. Do not freeze | Minimum 3ml peripheral blood in Sodium Heparin (green top) vacutainer |
|  | Peripheral blood | 3ml Blood in Sodium Heparin (green cap) vacutainer | Ambient Temperature. Do not freeze | Minimum 3ml in sodium heparin vacutainers |
| | Peripheral blood for CMA | 3ml Maternal/Whole Blood in EDTA Vacutainer | Ambient Temperature. Do not freeze | Minimum 3ml of blood in EDTA vacutainers |
|  | Product of Conception | Minimum 20 mg of Products of Conception | Ambient Temperature. Do not freeze | Minimum 20mg of tissue in sterile container in RPMI1640+1% Antibiotic. Cardiac/Cord or cord blood in Sodium Heparin Vacutainer |
| | Products of Conception for CMA | Tissue in Sterile Container with 10ml of sterile Normal Saline (1-2 drops of antibiotic after collection). Cardiac/Cord Blood in EDTA vacutainer | Ambient Temperature. Do not freeze | 200mg of tissue should be cleaned and collected in Saline. |
|  | Semen | 4 semen slides | Ambient Temperature. Do not freeze | 4 semen slides (Air dried packed face to face) or 1ml semen sample |

[8] David T. Miller, Margaret P. Adam, Swaroop Aradhya, et al. “Consensus Statement: Chromosomal Microarray Is a First-Tier Clinical Diagnostic Test for Individuals with Developmental Disabilities or Congenital Anomalies” The American Journal of Human Genetics, Volume 86, Issue 5, Pages 749-764 (May 2010)

# Claria from MedGenome offers the complete range of Reproductive Testing solutions

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