CONSENT FOR CHROMOSOMAL MICROARRAY ANALYSIS FOR PRENATAL DIAGNOSIS

INVITAE | CombiMatrix

Patient Name: _____ DOB: _____

Parent/Guardian Name: _____ Date: _____

Test Description and Limitations

1. Losses or gains of chromosomal information (copy number changes or "variants") can result in developmental delays, intellectual disability, autism spectrum disorders and/or birth defects. Chromosomal microarray analysis (CMA) evaluates copy number variants. In addition, CMA that uses single nucleotide polymorphism (SNP) probes can identify triploidy, molar pregnancies, and maternal cell contamination, as well as regions of homozygosity (ROH) that do not involve a copy number change, but may be associated with uniparental isodisomy and/or shared ancestry.
2. The CombiSNP™ Whole Genome Array for Prenatal Analysis uses SNP probes to evaluate the entire genome (all of the chromosomes) for copy number variants and copy-neutral ROH. This particular CMA test evaluates over 500 genes known to be associated with developmental disorders and/or birth defects, as well as over 2000 genes not currently known to be associated with any syndromes.
3. The CombiSNP™ Targeted Array for Prenatal Analysis uses SNP probes to target over 200 well-characterized regions of known clinical significance. This particular CMA adjusts probe coverage across regions not associated with known diseases in order to minimize the risk of identifying a variant of unclear clinical significance (VOUS), while maximizing coverage for regions of clinical significance. The CombiSNP™ Targeted Array will significantly reduce, but not eliminate, the chance of obtaining a VOUS. A complete list of the targeted regions and genes covered by the CombiSNP™ Targeted Array is available at http://combimatrix.com/targeted-array-v1.pdf.
4. Limitations of CombiSNP™ Whole Genome Array and the CombiSNP™ Targeted Array include the inability to detect: balanced chromosomal rearrangements, copy number variants below the stated resolution of the test, uniparental heterodisomy, and low level mosaicism. Also, CombiMatrix does not typically report carrier status for recessive disorders due to a deletion/duplication of a single gene or copy number changes identified in regions of no known or suspected clinical associations.

Test Results and Interpretation

1. An **Abnormal/Positive result** indicates the presence of one or more copy number variants that are known to cause a developmental disorder or abnormal phenotype, or the presence of a region of homozygosity (ROH), which may represent shared ancestry or the possibility of an imprinting disorder.
2. A **Normal/Negative result** indicates that no clinically significant copy number variants or ROHs were identified. Please note that:
   - An individual can have a normal microarray result and still have a genetic syndrome or chromosomal disorder.
3. A **Variant of Uncertain Significance (VOUS) result** typically indicates that a copy number variant has been identified that is not benign, but has also not been associated with any specific disorders. A VOUS result may also represent a copy number variant that is considered to be a risk factor for a developmental disorder/birth defect, but has also been identified in healthy individuals. Please note that:
   - Familial studies may or may not be helpful in further investigating the potential clinical significance of the variant.
   - If the individual tested is not a blood relative of the patient (i.e. misattributed paternity), this can lead to an inaccurate interpretation of the patient's results.

Confidentiality and Genetic Counseling

1. Test results will be released only to the referring physician, genetic counselor, reference laboratory, patient, or patient's personal representative in order to protect patient confidentiality.
2. No testing apart from that which is ordered by your physician will be performed on your sample. Additional testing requires the patient's/guardian's additional, express consent.
3. All samples are destroyed after 60 days, however, any remaining extracted DNA is retained for 5 years. You have the option of allowing CombiMatrix to completely de-identify the sample and strip it of all protected health information in order to use this sample for validation or educational purposes

   If you consent to the completely de-identified sample being used for laboratory validation and education purposes, please initial here:

   _____
4. Genetic counseling to discuss the benefits and limitations of CMA is recommended *prior* to testing. Once the CMA results are complete, genetic counseling is also recommended for results discussion. Depending upon the results of the CMA, further testing and/or diagnostic evaluations may be indicated.

Authorization for Chromosomal Microarray Analysis

I request and authorize CombiMatrix to perform a chromosomal microarray (CMA) on my/my child's sample. I understand the information above, and have had an opportunity to ask questions, which have been answered to my satisfaction.

X _____

Patient OR Parent/Guardian Signature Date

I have explained the benefits and limitations of CMA to this patient and/or legal guardian, and answered all questions.

X _____

Physician/Genetic Counselor Signature Date

As a participant in the International Consortium for Clinical Genomics (ICCG), CombiMatrix contributes de-identified clinical information and CMA results to a HIPAA-compliant public database, which is part of the National Institutes of Health's effort to improve our understand of the relationships between genetic variants and clinical symptoms. The confidentiality of each sample is maintained. If you do not wish to have your de-identified genomic information submitted to this database, please check the box below.

☐ I do not wish to provide this information to the ICCG database. (If the box is not marked, consent is implied.)