Dear Colleague,

This guide has been created as an educational tool to assist with your discussion of Prenatal Targeted Array analysis with your patients. It explains the combined CGH and SNP array platform used at GeneDx for detection of copy number changes and uniparental disomy, respectively. It is designed such that one side of the booklet is intended as the patient view, and the opposing page contains information for the practitioner. Pages for the patient are designated with the word “Patient” at the top right corner of the page. This guide also contains a separate Practitioner’s Section including an overview of the prenatal testing services available at GeneDx, and a more detailed overview of the GeneDx Prenatal Targeted Array testing service.

We hope that this guide provides you and your patients with a better understanding of the GeneDx Prenatal Targeted Array.

Sincerely,

The GeneDx Team
Information for the Patient
The GeneDx Prenatal Targeted Array screens for 100 clinically defined microdeletion and microduplication syndromes*, imbalances >1.5 Mb genome-wide, and uniparental disomy.

The sensitivity of array CGH is 10-15% higher than conventional cytogenetic testing in individuals with developmental delay, mental retardation, and/or multiple congenital anomalies (Miller et al., Am J Hum Genet 86:749-764, 2010). The sensitivity of array CGH in prenatal settings is also expected to be high, and the American College of Obstetrics & Gynecology has recommended targeted array CGH testing for fetuses with abnormal ultrasound findings (ACOG Committee Opinion No. 446. Obstet & Gynecol 114:1161-1163, 2009).

Below are indications for ordering a GeneDx Prenatal Targeted Array:

- Abnormal fetal ultrasound findings
- Ambiguous karyotype results
- Suspected deletion/duplication syndrome
- Suspected disorder caused by uniparental disomy (UPD)
- Family history of known or suspected chromosome imbalances

*For complete list of targeted regions, refer to page 37
There is a new improved test available for diagnosis of chromosome abnormalities known as the GeneDx Prenatal Targeted Array. This microarray analyzes genetic material for 100 syndromes that typically cannot be detected by standard chromosome analysis, loss or gains of chromosomal material from small changes to the length of an entire chromosome, as well as unusual inheritance of genetic material from parents.

Below are indications for ordering a GeneDx Prenatal Targeted Array:

- Abnormal ultrasound findings
- Ambiguous chromosomal structure
- Suspected loss or gain of genetic material in the fetus
- Suspected disorder caused by genetic material received from only one parent (uniparental disomy or UPD)
- Family history (or suspicion) of diseases caused by genetic anomalies
Our bodies are made up of millions of cells. Each cell typically contains 2 sets of 23 chromosomes, 1 set inherited from the mother and the other from the father. Each chromosome has many genes which contain all essential information for growth and development.
Too much or too little genetic material can cause abnormal growth and development. Traditional chromosome analysis can identify the following:

**Extra Chromosome**

![Extra Chromosome Image]

**Missing Chromosome**

![Missing Chromosome Image]

**Large Deletion on a Chromosome**

![Large Deletion Image]

**Large Duplication on a Chromosome**

![Large Duplication Image]
Too much or too little genetic material (copy number changes) or abnormal inheritance of genetic material from parents can cause developmental diseases. GeneDx Prenatal Targeted Array is a very sensitive test to detect these types of genetic defects.

Deletion: Too little genetic material

Duplication: Too much genetic material
In addition, this microarray can also detect abnormal inheritance of genetic material from parents (uniparental disomy). Uniparental disomy (UPD) occurs when both chromosomes in a pair, or part of a chromosome, are inherited from one parent and there are no copies inherited from the other parent. UPD is a random, rare event that happens in the formation of an egg or sperm, or very early in fetal development. In the majority of cases, UPD causes no abnormalities, however some occurrences of UPD may result in a specific genetic disorder. The GeneDx Prenatal Targeted Array can detect UPD on chromosomes 6, 7, 11, 14, 15, 20, and X. Abnormal inheritance of these chromosomes exclusively from one parent can cause genetic disorders.
What can the GeneDx Prenatal Targeted Array find?

- Too few (monosomy) or too many (trisomy) chromosomes
- Deletions (500 bp - 100 kb in 100 targeted regions and 1.5 Mb or larger in the rest of the genome)
- Duplications (500 bp - 100 kb in 100 targeted regions and 1.5 Mb or larger in the rest of the genome)
- Small deletions or duplications of individual exons within select single genes (intragenic mutations)
- The chromosomal origin of ambiguous karyotype results (e.g. marker chromosomes, ring chromosomes, suspected chromosomal rearrangements)
- Accurate boundaries of deletions or duplications to help define which genes may be of clinical significance
- Uniparental disomy (UPD) on chromosomes 6, 7, 11, 14, 15, 20, and X.
- Evidence suggesting a close genetic relationship between the mother and father of the pregnancy being tested (consanguinity or shared ancestry)

What can the GeneDx Prenatal Targeted Array not find?

- Balanced rearrangements such as balanced robertsonian or reciprocal translocations, balanced insertions, and inversions (detectable by traditional karyotyping and FISH analysis only)
- Low-level mosaicism (<25%)
- Genomic imbalances in regions that are not represented on the array
- Small DNA mutations such as point mutations, small intragenic deletions or insertions (detectable by DNA sequencing only)
What can the GeneDx Prenatal Targeted Array find?

- Too few chromosomes (case example: Turner syndrome or Monosomy X)
- Too many chromosomes (case example: Down syndrome or Trisomy 21)
- Loss of genetic material known as deletions (ranging in size from very small to very large)
- Gain of genetic material known as duplications (ranging in size from very small to very large)
- Identification of genes lost or gained and the associated genetic disorder
- Genetic disorders caused by uniparental disomy
- Evidence suggesting a close genetic relationship between the mother and father of the pregnancy being tested (consanguinity or shared ancestry)

What can the GeneDx Prenatal Targeted Array **not** find?

- Chromosomal changes that do not result in a gain or loss of genomic material
- Small deletions or duplications that are within chromosomal regions not represented on the array
- Small DNA changes that require a different test method called “DNA sequencing”
How Is It Done?

Step 1

- Prenatal specimen is obtained through chorionic villi sampling (CVS), amniocentesis, or percutaneous umbilical blood sampling (PUBS) procedure
- Fetal DNA is isolated from direct or cultured prenatal specimen
- Fetal DNA is tagged with red fluorescent dye
- Control DNA is tagged with green fluorescent dye
How Is It Done?

Step 1

Fetal DNA is extracted from the prenatal specimen (*see specimen requirements on page 43)

Fetal DNA is labeled or “tagged” with a red fluorescent label

Control DNA is labeled or “tagged” with a green fluorescent label
How Is It Done?

- The fetal DNA is extracted and combined with the control DNA
- The combined DNA is hybridized to the GeneDx Prenatal Targeted Array
- The array is a glass slide coated with 42,000 specifically selected CGH oligonucleotide probes placed throughout the genome and within 100 targeted common and novel microdeletion/microduplication syndromes, and an additional 18,000 SNP probes covering chromosomes 6, 7, 11, 14, 15, 20 and X.
- During hybridization, fluorescently “tagged” pieces of fetal DNA and the control DNA attach to the probes with complementary sequences.
How Is It Done?

Step 2

A

At each spot, custom-made DNA probes are fixed to the prenatal array slide

Side view of DNA probes attached at each spot

B

Tagged DNA is applied to the prenatal array slide

Pipette with combined fetal and control DNA

C

Top view of prenatal array slide

“tagged” pieces of fetal DNA and control attach to the probes
After incubation, the analysis instrument determines how much red (fetal DNA) and green (control DNA) is attached to each of the spots on the array.

The ratio of red to green signals are displayed:

- **Yellow** = Equal amounts of fetal and control DNA = Normal result
- **Red >> Green** = Genomic gain in fetal DNA = duplication or trisomy
- **Red << Green** = Genomic loss in fetal DNA = deletion or monosomy

In addition, at some spots on the array the intensity of the fluorescence signal can provide information about the parental origin of chromosomal material (SNP analysis).
Analysis

Actual GeneDx Prenatal Targeted array slide has 66,000 DNA probes to identify abnormal genetic structure and inheritance.

Analysis instrument

Normal Result
Equal amounts of red and green signals

Genomic Gain (duplication)
Too much red signal

Genomic Loss (deletion)
Too much green signal
Possible Result Outcomes
Negative result is illustrated by:

- Similar amount of fetal and control DNA present (yellow dots)
- Normal CGH result is represented by an even signal distributed on the baseline along the length of the entire chromosome; indicating no gain or loss of genetic material.
- Normal SNP result is represented by the presence of signals distributed into three lines along the length of the entire chromosome, reflecting normal inheritance of genetic material from both parents.
Typical Pattern of Negative GeneDx Prenatal Targeted Array

Normal amount of DNA (2 copies) appears as “yellow” spots on array

Fluorescence from hundreds of spots are measured and graphically lined up to depict one whole chromosome

Normal CGH results seen as even signal through baseline along the length of the chromosome

Normal SNP results seen as signals distributed into three lines along the length of the chromosome.
Many genetic conditions cannot be diagnosed by GeneDx Prenatal Targeted Array

- Discuss further testing to look for mutations within a single gene (sequencing) if a specific disorder/syndrome is suspected based on fetal ultrasound abnormalities
- Discuss karyotype analysis to look for balanced chromosome abnormalities
- Some disorders are multi-factorial, and other genetic and environmental factors could be considered
- Not all causes of a fetal ultrasound abnormalities can be identified with today’s testing technologies

- Continued follow-up with your prenatal health care team
- Appropriate prenatal follow-up and management
- Postnatal clinical evaluation of newborn and appropriate genetic evaluation
Genomic deletion is illustrated by:

- Loss of fetal DNA compared to the control
- **Green** dot on the array diagram
- “Dip” on the CGH chromosome array plot
Typical Pattern of a Genomic Deletion

Probes in deleted region appear as “green” dots on array

Deletion seen as “dip” in signal intensity
Typical Pattern of a Genomic Duplication

Genomic duplication is illustrated by:

- Additional copy of fetal DNA compared to the control DNA
- **Red** dot on the array diagram
- “Jump” in the CGH chromosome array plot
Typical Pattern of a Genomic Duplication

Probes in deleted region appear as “red” dots on array

Duplication seen as “jump” in signal intensity
Exon-level copy number analysis in individual genes

- The GeneDx prenatal array can detect small deletions or duplications of individual exons in genes associated with Mendelian disorders that are detectable prenatally (see appendix).
- The array contains dense probe coverage in all exons of select genes to maximize detection sensitivity.
- Nine genes are targeted at the exon level, including SRY, SOX9, MECP2, L1CAM, DHCR7, SOX2, SALL1, SALL4, and IL1RAPL1.
Exon-level copy number analysis of individual genes

The GeneDx array contains dense probe coverage in all coding portions (exons) of select genes that are important prenatally.

Single exon deletion seen as “dip” in signal intensity
Typical Pattern of Uniparental Disomy

(Case example: Prader-Willi syndrome)

Segmental uniparental disomy for chromosome 15 is illustrated by:

- Normal copy number for chromosome 15 illustrated by an even signal along the entire chromosome 15 on the CGH array chromosome graph
- Abnormal SNP array chromosome graph showing absence of signal on middle line (absence of paternal contribution on part of chromosome 15), indicating abnormal parental inheritance.
Typical Pattern of Uniparental Disomy (UPD)

Case Example: Prader-Willi syndrome (PWS) is a genetic disorder characterized by developmental delay, low muscle tone, characteristic facial features, and feeding difficulties in infancy followed by excessive eating and obesity in childhood/adulthood. Approximately 25-30% of PWS cases are caused by maternal uniparental disomy for chromosome 15.

Normal CGH results seen as even signal through baseline along the length of the chromosome 15

Abnormal SNP results indicating abnormal parental inheritance, or maternal UPD, for part of chromosome 15 (Prader-Willi critical region)
A positive or variant of unknown significance is identified

What’s next?

- Result confirmation – the abnormal result is confirmed by FISH analysis, quantitative PCR (qPCR), or repeat array analysis
- FISH analysis is performed to determine the chromosomal mechanism for the imbalance, qPCR is used to confirm small aberrations (<1 Mb deletions or duplications), and repeat array analysis is used to confirm multiple chromosomal imbalances, UPD or consanguinity
- Parental samples (if available) are evaluated concurrently with the fetal sample, using the same method
- Abnormal test results are reported out directly to the ordering practitioner(s) by a GeneDx genetic counselor
Positive Test Result

Deletion/duplication of genetic material or abnormal parental inheritance identified

What’s Next

- Testing of parents recommended to establish recurrence risk, to determine mechanism of chromosomal imbalance, and to determine if UPD is maternal or paternal
- Discuss prenatal test results and pregnancy management options
- Testing of other family members is available
Variants of Unknown Clinical Significance

The GeneDx Prenatal Targeted array design ensures high sensitivity while limiting the possibility of identifying genetic abnormalities that cannot be interpreted from a clinical perspective – very important in a prenatal setting.

A variant of unknown clinical significance is defined as a deletion/duplication of DNA identified that may or may not be associated with the clinical features because:

- There are no previous reports of deletions/duplications in this region
- The abnormality is very small
- The abnormality might be a normal variation in the family and/or general population
- The relationship between the genes in the deletion/duplication region and the clinical features is unknown

Need more information

(Continued on next page)
Variants of Unknown Clinical Significance

Need more information

Testing of both parents is necessary

Unaffected parent also has the same del/dup

Parents do not have the del/dup

Parent is affected and also has the same del/dup

Parents not available for testing

Del/dup is most likely a normal variant in the family and is not associated with the fetal condition

Del/dup has newly occurred in the fetus and is more likely to be associated with the fetal condition

Del/dup is inherited and is likely to be associated with the condition occurring in the family

No further interpretation possible

Future research and/or case studies may provide a better understanding of this result

Continued prenatal follow-up and management is recommended

Parents do not have the del/dup

Parent is affected and also has the same del/dup

Parents not available for testing

Future research and/or case studies may provide a better understanding of this result

Continued prenatal follow-up and management is recommended

No further interpretation possible
Other GeneDx Prenatal Tests
# Prenatal Testing for Fetuses with Increased Nuchal Translucency

## Relevant Published Information about Genetic Testing in Fetuses with Increased Nuchal Translucency

### Aneuploidies:
- Trisomy 21, 13, 18, Monosomy X
  - **Testing at GeneDx**: Chromosome analysis
  - **Relevant Published Information**: Positive in 20% of fetuses with NT of 4.0 mm to 65% with NT of >6.5 mm (Ref 1)

### DiGeorge/VCF Syndrome
- **Testing at GeneDx**: Chr. 22q11.2 FISH, Prenatal targeted microarray (see below)
  - **Relevant Published Information**: FISH/MLPA: 0/146 Fetuses positive for 22q11.2 deletion/duplication; frequency estimated between 0-2.7% (Ref 2)
    - Primer extension assay to test for 22q11.2 deletion (17 selected probes in 7 genes within the deletion region):
      - 0/120 (0%) Fetuses positive for 22q11.2 deletion (Ref 3)

### Microdeletion/duplication syndromes and subtelomeric deletions, other large (>1.5Mb) copy number aberrations anywhere in the genome
- **Testing at GeneDx**: Prenatal targeted microarray
  - **Relevant Published Information**: Adverse outcome (anomalies, miscarriages, TOP, fetal death) reported in 2.1% - 21% of all pregnancies; mean: 10.6% (Ref 4)
  - Pathogenic copy number aberrations detected by array CGH in 12% of fetuses with INT (Ref 5)

### Noonan syndrome
- **Testing at GeneDx**: Concurrent full gene sequencing of 8 genes (PTPN11, RAF1, SOS1, KRAS, HRAS, BRAF, MAP2K1, MAP2K2), targeted testing for recurrent SHOC2 mutation
  - **Relevant Published Information**: Analysis of PTPN11: 12/134 (9%) Fetuses positive for PTPN11 mutation (Ref 6, including GeneDx data)
    - Analysis of 71 selected mutations in 5 genes: 8/120 (6.6%) Fetuses positive (Ref 3)
    - Analysis of 8+ genes: (GeneDx unpublished data) 9/117 (7.6%) Fetuses positive for a mutation

### Smith-Lemli-Opitz Syndrome, CHARGE Syndrome, Androgen Insensitivity Syndrome, EEC Syndrome, Holoprosencephaly
- **Testing at GeneDx**: Full gene sequencing or targeted gene sequencing, and deletion/duplication analysis if indicated
  - **Relevant Published Information**: Rare case reports of disorder associated with increased NT (Ref 1, 3, 4)

### Spinal muscular atrophy, Congenital adrenal hyperplasia
- **Testing at GeneDx**: Parental carrier testing available elsewhere
  - **Relevant Published Information**: Rare case reports of disorder associated with INT (Ref 1, 4, 7)
    - 0/120 (0%) Fetuses positive for a mutation (Ref 3)
    - 9/120 (7.5%) Fetuses heterozygous carriers for SMA (Ref 3)

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Increased Nuchal Translucency

- Increased nuchal translucency (NT) at 11-14 weeks of pregnancy can indicate the presence of one of >50 genetic disorders.

- The most common cause is an extra or a missing chromosome (‘chromosomal aneuploidy’), which can be identified by chromosome analysis, FISH or prenatal microarray analysis.
  - Trisomy 13 and trisomy 18 or monosomy X (Turner syndrome) seen with lower frequency.

- The most common single-gene disorder associated with increased NT is Noonan syndrome.

- In a fetus with increased NT, the frequency of other genetic disorders is very low.
Prenatal Testing For Noonan Syndrome

- Autosomal dominant mutations in at least 9 different genes are known to cause Noonan syndrome or related disorders with overlapping features.
  - The ‘Prenatal Noonan Panel’ at GeneDx simultaneously analyzes the sequence of eight genes (PTPN11, RAF1, SOS1, KRAS, HRAS, BRAF, MAP2K1, MAP2K2) and one recurrent mutation (SHOC2).
  - Using this panel, 7.6% of fetuses with increased NT and/or other ultrasound abnormalities tested POSITIVE for a published mutation in these genes.
  - 75% of fetuses (9/12) with a disease-causing mutation in PTPN11 had other ultrasound abnormalities with or without increased NT (Lee at al. Clin Genet 75:190-194, 2009)
- Prenatal Noonan syndrome testing is at present the only single-gene disorder test with significant diagnostic relevance for increased NT.
Prenatal Testing For Noonan Syndrome

- Noonan syndrome is an autosomal dominant disorder mainly characterized by short stature, congenital heart defects, characteristic facial features. The clinical features can be highly variable, even within a family.

- Certain fetal ultrasound findings, such as cystic hygroma, increased nuchal translucency and fetal hydrops, have been observed in individuals with Noonan syndrome.

- Autosomal dominant mutations in at least 9 different genes are known to cause Noonan syndrome or related disorders with overlapping features.

- The ‘Prenatal Noonan Panel’ at GeneDx simultaneously analyzes the sequence of eight genes (PTPN11, RAF1, SOS1, KRAS, HRAS, BRAF, MAP2K1, MAP2K2) and one recurrent mutation in the SHOC2 gene.

- Prenatal Noonan syndrome testing is at present the only single-gene disorder test with significant diagnostic relevance for increased NT.
What Other Molecular Prenatal Tests Can be Ordered from GeneDx?

- Targeted Prenatal Testing for Known Familial Mutation(s)
- Prenatal Genetic Tests Based Abnormal Ultrasound Findings

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<tr>
<th>Ultrasound presentation</th>
<th>Disorder</th>
<th>Genes</th>
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<td>Limb and extremity abnormalities</td>
<td>EED / SHFM / Hay-Wells syndrome</td>
<td>TP63</td>
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<tr>
<td>Upper limb malformations and/or heart defects</td>
<td>Holt-Oram syndrome</td>
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<tr>
<td>Fetal renal malformations and abnormalities of the limbs and extremities</td>
<td>Townes-Brocks syndrome or Duane-Radial-Ray syndrome / Acro-renaloocular syndrome</td>
<td>SALL1 and SALL4</td>
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<tr>
<td>Shortening and bowing of the long bones, ambiguous genitalia, and/or increased NT</td>
<td>Campomelic dysplasia</td>
<td>SOX9</td>
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<td>Ambiguous genitalia or gender inconsistent with karyotype</td>
<td>Disorder of sex development or androgen insensitivity</td>
<td>SRY or AR</td>
</tr>
<tr>
<td>Abnormal biochemical screen, IUGR, malformations, ambiguous genitalia</td>
<td>Smith Lemli Opitz</td>
<td>DHCR7</td>
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<tr>
<td>Hydrocephalus and/or aqueductal stenosis</td>
<td>X-linked hydrocephalus / MASA</td>
<td>L1CAM</td>
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<tr>
<td>Holoprosencephaly, cleft lip/palate, or hydrocephalus</td>
<td>Holoprosencephaly</td>
<td>TGIF, SHH, SIX3, and ZIC2</td>
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<tr>
<td>Heart defects, CNS malformations, renal/GI malformations, cleft lip/palate</td>
<td>CHARGE syndrome</td>
<td>CHD7</td>
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<tr>
<td>Cystic hygroma, increased NT, cardiac defects, lymphedema, macrosomia, or polyhydramnios</td>
<td>Noonan syndrome</td>
<td>9 gene panel</td>
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<tr>
<td>Abnormal inter- or intra-globe distance or missing globes</td>
<td>Anophthalmia or microphthalmia</td>
<td>SOX2, OTX2, and VSX2</td>
</tr>
</tbody>
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Quick Review: GeneDx Prenatal Targeted Array

What is the GeneDx Prenatal Targeted Array?
• The Prenatal Targeted array is a combined CGH and SNP array platform for detection of copy number changes and uniparental disomy, respectively.
• The array is a glass slide coated with 42,000 specifically selected CGH probes placed throughout the genome and within 100 targeted common and novel microdeletion/microduplication syndromes, and an additional 18,000 SNP probes covering chromosomes 6, 7, 11, 14, 15, 20, and X. Exon-level probe coverage is added to some genes associated with Mendelian disorders that are detectable prenatally.
• Probes are placed at an average spacing of 450 kb across the unique sequence of the genome and at 200 bp-25 kb in targeted loci (e.g., subtelomeric or microdeletion/microduplication syndrome regions)

Prenatal Comparative Genomic Hybridization and Single Nucleotide Polymorphism Array Analysis (CGH + SNP array)
• The GeneDx prenatal targeted array is a diagnostic test that can identify regions of gain or loss of genetic material across the entire human genome (with the exception of centromeres and satellites). Additionally, SNP analysis can identify uniparental disomy.

• The GeneDx prenatal targeted array is a test in which fetal DNA and control DNA are fluorescently labeled and hybridized to an array of 60,000 oligonucleotides.
• Copy number analysis is performed by comparing the amount of fetal and control DNA, and mapping this against the genome.
• In addition, at some spots on the array the intensity of the fluorescence signal can provide information about the parental origin of chromosomal material (SNP analysis).

When to use the GeneDx Prenatal Targeted Array?
• The American College of Obstetrics & Gynecology has recommended targeted array CGH as a preliminary test for fetuses with abnormal ultrasound findings (ACOG Committee Opinion No. 446. Obstet & Gynecol 114:1161-1163, 2009).
• As a preliminary test when fetal ultrasound abnormalities are suggestive of a specific deletion/duplication disorder or of a specific disorder caused by uniparental disomy.
• As a preliminary test when there is a known familial chromosome abnormality.
• As a secondary test following abnormal or ambiguous karyotype results.
What Can the GeneDx Prenatal Targeted Array Find?

- Too few (monosomy) or too many (trisomy) chromosomes
- Deletions (500bp - 100 kb in 100 targeted regions and 1.5 Mb or larger in the rest of the genome)
- Duplications (500bp - 100 kb in 100 targeted regions and 1.5 Mb or larger in the rest of the genome)
- Deletions or duplications of individual exons in some targeted genes
- The chromosomal origin of ambiguous karyotype results (e.g. marker chromosomes, ring chromosomes, suspected chromosomal rearrangements)
- Accurate boundaries of deletions or duplications to help define which genes may be of clinical significance
- Uniparental disomy (UPD) on chromosomes 6, 7, 11, 14, 15, 20, and X
- Evidence suggesting a close genetic relationship between the mother and father of the pregnancy being tested (consanguinity or shared ancestry)

What Can the GeneDx Prenatal Targeted Array Not Find?

- Balanced rearrangements such as reciprocal translocations, balanced insertions, and inversions (detectable by traditional karyotyping and FISH analysis only)
- Low-level mosaicism (<25%)
- Genomic imbalances in regions that are not represented on the array
- Small DNA mutations such as point mutations, small intragenic deletions or insertions (detectable by DNA sequencing only)

Why should the parents of the fetus be tested?

- Testing the parents will help determine the recurrence risk by identifying the mechanism of the chromosomal imbalance, and to determine if uniparental disomy is maternal or paternal.
- If a variant of unknown significance is identified in the fetus, testing the parents can provide information on whether the variant is disease causing or likely benign.
How To Order GeneDx Prenatal Targeted Array

For GeneDx Prenatal Targeted Array please submit the following information:

1. Prenatal Genetic Testing sample submission form
2. Payment options / Institutional Billing form (Page 3 of submission form)
3. Informed consent (Page 4 of submission form)
4. Please **legibly print the reporting physician contact information**
5. **Complete the Clinical Information Form**
   - It is important to provide the lab with as much clinical information as possible.
   - For optimal result interpretation, it is critical to relate the fetal ultrasound findings to the genes present in the detected imbalance.

- Specimen requirements: 20 mL direct amniotic fluid, 20 mg chorionic villi, or 2 T25 flasks of cultured cells (CV or amniocytes) or 3 ug fetal DNA.
- Maternal blood (1-5 ml in a lavender-top EDTA tube) is required for maternal cell contamination (MCC) studies. The maternal sample should accompany the prenatal specimen or be shipped to arrive prior to or concurrently with the prenatal sample.
- Submitting a paternal sample at the same time as the maternal sample is **strongly recommended** for faster turn-around-time when follow-up parental testing is performed for result interpretation.
- If more than one prenatal test is ordered, 30 mL amniotic fluid, 30 mg villi or 3 T25 flasks of cultured cells are requested.
- If insufficient material is received, particularly for direct amniotic fluid or chorionic villi, cells will need to be cultured. This will increase turn-around-time.
- Ship the specimen(s) **overnight at ambient temperature**, using a cool pack in hot weather.
- To download the GeneDx information sheet and submission form please visit our website at www.GeneDx.com/prenatal
- Also, for further assistance please call us at (310) 519-2100 or email us at prenatal@genedx.com
## Genomic regions assayed by prenatal targeted array CGH:

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<td>1q43-1q44 microdeletion</td>
<td>1q43-1q44</td>
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<td>2p15 microdeletion</td>
<td>2p15-2p16.1</td>
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<td>2q33 microdeletion</td>
<td>2q32.2-2q33</td>
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<tr>
<td>2q37 microdeletion</td>
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<tr>
<td>3q29 microdeletion</td>
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<tr>
<td>6p25 microdeletion (including FOXC1)</td>
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<tr>
<td>7q11 Williams region duplication</td>
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<td>12q14.13 microdeletion</td>
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<td>17q21 microdeletion/duplication</td>
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<td>22q11 VCF/DOS deletion and reciprocal duplication</td>
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<td>Hereditary neuropathy with pressure palsies</td>
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## Syndrome | Locus |
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<td>Miller-Dieker syndrome</td>
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<td>Prader-Willi syndrome</td>
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