**Prequel™ Prenatal Screen**

**RESULTS SUMMARY**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Results</th>
<th>Patient-specific PPV or Residual Risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21 (Down Syndrome)</td>
<td>POSITIVE: PREGNANCY AT INCREASED RISK Aneuploidy suspected (borderline value) Results suggestive of trisomy for chromosome 21.</td>
<td>81.71% (81.71 in 100) PPV</td>
</tr>
<tr>
<td>Trisomy 13 (Patau Syndrome)</td>
<td>NEGATIVE Results consistent with two copies of chromosome 13.</td>
<td>&lt; 0.01% (1 in 10,000) Residual Risk</td>
</tr>
<tr>
<td>Trisomy 18 (Edwards Syndrome)</td>
<td>NEGATIVE Results consistent with two copies of chromosome 18.</td>
<td>&lt; 0.01% (1 in 10,000) Residual Risk</td>
</tr>
</tbody>
</table>

**NEXT STEPS**

Genetic counseling is recommended.

**CLINICAL NOTES**

* The positive predictive value (PPV) represents the risk for the pregnancy to be affected with the indicated chromosome anomaly in view of a positive result. The residual risks provided represent the remaining chance that the pregnancy is affected with the indicated chromosome anomaly in view of a negative result.

This is a screening test; therefore, false positive and false negative results can occur. Clinical correlation with ultrasound findings and history is indicated. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis is necessary.
POSITIVE: PREGNANCY AT INCREASED RISK
Trisomy 21 (Down Syndrome)

<table>
<thead>
<tr>
<th>Patient</th>
<th>SHANON DOLAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>Aneuploidy suspected (borderline value)</td>
</tr>
<tr>
<td>Methodology</td>
<td>Sequencing with fetal aneuploidy analysis (v2.2)</td>
</tr>
<tr>
<td>Interpretation</td>
<td>Results suggestive of trisomy for chromosome 21.</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>81.71% (81.71 in 100)</td>
</tr>
</tbody>
</table>

What is Down syndrome?

Most individuals with Down syndrome, called trisomy 21, have an extra copy of chromosome 21 in the cells of the body. This extra genetic material causes changes in development of the embryo and fetus resulting in physical and developmental changes.

IQ typically ranges from mild to moderate intellectual disability. Health conditions can include low muscle tone, heart defects, intestinal issues and vision or hearing conditions. While the average life expectancy for a person with Down syndrome is 60 years, health conditions like those mentioned above may result in a shorter life expectancy.

Each person with Down syndrome is unique and the severity of the symptoms varies greatly among individuals. Outcomes for people with Down syndrome have improved significantly in the past 40 years with increased access to education, social supports, employment opportunities, and family support.

How common is Down syndrome?

Down syndrome occurs in about 1 in 800 live births. The condition is not related to race, nationality, religion or socioeconomic status. There is usually no family history of Down syndrome.

How is trisomy 21 (Down syndrome) treated?

There is no single, standard treatment for Down syndrome. Treatments are based on each individual’s physical and intellectual needs as well as his or her personal strengths and limitations.

Individuals with Down syndrome may receive care from a team of health professionals, including physicians, special educators, speech therapists, occupational therapists, physical therapists, and social workers.
REFERENCES


Resources

LETTERCASE.ORG | http://lettercase.org
The Kennedy Foundation's Understanding a Down Syndrome Diagnosis book (lettercase.org) is intended for patients whose pregnancy has an increased chance for a prenatal diagnosis of Down syndrome. This book includes basic information about Down syndrome; potential medical conditions; available supports; reproductive options; and resources about Down syndrome, and it was prepared with assistance by representatives of the national medical and Down syndrome organizations and is recommended in the guidelines of the major genetics organizations.

Human Development Institute
126 Mineral Industries Bldg.
University of Kentucky
Lexington, KY 40506-0051
Phone: 404-828-0290
info@lettercase.org

NATIONAL DOWN SYNDROME CONGRESS | http://www.ndsccenter.org
Since 1973 NDSC has worked to "provide information, advocacy and support concerning all aspects of life for individuals with Down syndrome."
1370 Center Drive, Suite 102, Atlanta, GA 30338
Phone: 800-232-NDSC (6372)

NATIONAL DOWN SYNDROME SOCIETY | http://www.ndss.org/
NDSS is a national advocacy organization working "for the value, acceptance and inclusion of people with Down syndrome."
666 Broadway, New York, NY 10012
Phone: 800-221-4602
Methods and Limitations

**Methodology:** Sequencing with fetal aneuploidy analysis.

**Conditions Tested:** Chromosome 13 Aneuploidy, Chromosome 18 Aneuploidy, and Chromosome 21 Aneuploidy.

Sequencing with fetal aneuploidy analysis

Nucel acid extraction and DNA sequencing are used to determine fetal aneuploidy. This test is designed to detect chromosome aneuploidies and is validated for chromosomes 1-22, X and Y. The test is validated for singleton and twin pregnancies with gestational age of at least 10 weeks as estimated by last menstrual period. These results do not eliminate the possibility that this pregnancy may be associated with other chromosomal or subchromosomal abnormalities, birth defects and other conditions. This test is not intended to identify pregnancies at risk for open neural tube defects. A negative test result does not demonstrate the absence of chromosomal abnormalities such as trisomy 21, trisomy 18, trisomy 13, other autosomal aneuploidies, monosomy X, XXX, XXY, and XYY. The individualized residual risks and PPV are calculated from the test performance and prevalence based upon the provided gestational age and maternal age (or age of ovum donor, if available) for trisomy 13, trisomy 18, and Down syndrome. Twin PPV and residual risk calculations additionally incorporate prevalence of both monogygotic and dizygotic scenarios, regardless of individual status. Monosomy X PPV is calculated from test performance and prevalence based upon the provided gestational age. When an "aneuploidy detected" result is reported in a twin pregnancy, the status of each individual fetus cannot be determined. Although the presence or absence of Y chromosome material can be reported in a twin pregnancy, the occurrence of sex chromosome aneuploidies such as monosomy X, XXX, XXY and XYY cannot be evaluated in twin pregnancies. Autosomal aneuploidies of chromosomes other than 21, 18, and 13 cannot be evaluated in twin pregnancies. Confined placental mosaicism or maternal mosaicism, if present, may cause the test results to be inaccurate.

**Prenatal test performance data**

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Chromosome</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>99.7% (99.1 - 99.9)</td>
<td>99.96% (99.93 - 99.98)</td>
<td>Monosomy X</td>
<td>95.8% (70.3 - 99.5)</td>
<td>99.86% (99.62 - 99.95)</td>
</tr>
<tr>
<td>21 (twins)</td>
<td>98.6% (92. - 100)</td>
<td>99.96% (99.93 - 99.98)</td>
<td>XX</td>
<td>97.6% (94.8 - 99.1)</td>
<td>99.2% (97.2 - 99.9)</td>
</tr>
<tr>
<td>18</td>
<td>97.9% (94.9 - 99.1)</td>
<td>99.96% (99.93 - 99.97)</td>
<td>XY</td>
<td>99.1% (96.9 - 99.9)</td>
<td>98.9% (96.9 - 99.8)</td>
</tr>
<tr>
<td>13</td>
<td>99.0% (65.8 - 100.0)</td>
<td>99.96% (99.93 - 99.98)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

XXX/XXX/XXY Other sex aneuploidies will be reported if detected. (Limited data for these less common aneuploidies preclude performance calculations.)

Sex chromosome mosaicism cannot be distinguished by this method (the occurrence of which is <0.3%). Patients with such mosaicism will have a sex chromosome result reported and will fall into one of six categories (Monosomy X, XXX, XXY, XY, XX, XY).

15q11.2 deletion, 1p36 deletion syndrome, 22q11.2 deletion syndrome, 4p deletion, 5p deletion When requested, the listed microdeletions will be reported if detected. (Limited data for these rare subchromosomal anomalies preclude performance calculations.)

Expanded autosomal aneuploidies When requested, autosomal aneuploidies of chromosomes other than 21, 18, 13 will be reported if detected. (Limited data for these aneuploidies preclude performance calculations.)

Note: the above test performance statistics refer to singleton pregnancies unless otherwise stated.

**References**

• Illumina, Inc. Analytical Validation of the verifi® prenatal test: Enhanced Test Performance for Detecting Trisomies 21, 18, and 13 and the Option for Classification of Sex Chromosome Status. 2012.

Limitations

Possible sources of diagnostic error include sample mix-up, trace contamination, bone marrow transplantation, chimerism or mosaicism, and technical errors. This test was developed and its performance characteristics determined by Myriad Women's Health, Inc. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. These results are adjunctive to the ordering physician's evaluation and should be interpreted in the context of all available clinical findings. CLIA Number: #05D1102604.