



# Comprehensive screening for clearer insight

Noninvasive cell-free DNA  
(cfDNA) prenatal screening  
for your obstetric patients

**QNatal™ Advanced**  
Noninvasive Prenatal Screening

# Get advanced insight from comprehensive, validated technology

QNatal Advanced is a noninvasive cfDNA prenatal screening tool that can provide physicians and patients with a safe way to screen for chromosomal abnormalities in pregnancies.

## See how innovation translates to deeper insights

QNatal Advanced, an automated noninvasive prenatal screening assay, demonstrates excellent performance characteristics, high positive predictive values and very low “no-call” rates. Its validated technology delivers accurate results with clear positive or negative reporting for the following chromosomal abnormalities:

### Trisomies

Trisomy 21	Down syndrome
Trisomy 18	Edwards syndrome
Trisomy 13	Patau syndrome

### Fetal sex chromosomes

Fetal sex*	
45,X	Turner syndrome†
47,XXY	Klinefelter syndrome†
47,XXX	Triple X syndrome†
47,XXY	XXY syndrome†

### Microdeletions\*†

22q	DiGeorge syndrome
5p	Cri-du-chat syndrome
1p36	1p36 deletion syndrome
15q	Angelman/Prader-Willi syndromes
11q	Jacobsen syndrome
8q	Langer-Giedion syndrome
4p	Wolf-Hirschhorn syndrome

\*Can opt out.

†Reported as an Additional Finding.


## Unparalleled sensitivity and specificity

QNatal Advanced showed high sensitivity and specificity in a study of 2,752 pregnant women<sup>1,2</sup>

Trisomy Screen	Sensitivity	Specificity
<b>Singletons (n=2637)</b>		
90 of 90 trisomy 21	>99.9%	>99.9%
30 of 30 trisomy 18	>99.9%	>99.9%
18 of 18 trisomy 13	>99.9%	>99.9%
1 of 1 sex aneuploidies	>99.9%	>99.9%
371 of 372 fetal sex	>99.7% accuracy	
<b>Twins (n=115)</b>		
10 of 10 trisomy 21	>99.9%	>99.9%
4 of 4 trisomy 18	>99.9%	>99.9%
1 of 1 trisomy 13	>99.9%	>99.9%

## Simple and clear results reporting

- Obtain clear, direct Positive/Negative
- Very low no-call rate (0.88%)<sup>1</sup>


Report Status: Final  
TEST, TESTING

Patient Information	Specimen Information	Client Information
<b>TEST, TESTING</b> DOB: 01/01/1970    AGE: 44 Gender: F    Fasting: N Phone: NG Patient ID: NG	Specimen: SL006083J Requisition: 5032396 Lab Ref #: 5032396N Collected: 07/31/2014 / 09:00 PDT Received: 07/31/2014 / 09:14 PDT Reported: 08/06/2014 / 10:18 PDT	Client #: 97502840    AARRSSS TEST CLIENT (HQ) 1201 S COLLEGEVILLE RD COLLEGEVILLE, PA 19426-2998

QNatal Advanced™      Lab: SJC

**Interpretation Summary**

This specimen showed additional representation of chromosome 18 material consistent with Trisomy 18 (Edwards syndrome). Follow-up genetic counseling and diagnostic testing is suggested. An expected representation of chromosome 21 and 13 and X material was seen.

Chromosome Results	Fetal Sex Result	Pregnancy Data																				
<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Chromosome Tested</th> <th>Results</th> </tr> </thead> <tbody> <tr> <td>Trisomy 21 (T21)</td> <td>Negative</td> </tr> <tr> <td>Trisomy 18 (T18)</td> <td style="background-color: red; color: white;">Positive</td> </tr> <tr> <td>Trisomy 13 (T13)</td> <td>Negative</td> </tr> </tbody> </table>	Chromosome Tested	Results	Trisomy 21 (T21)	Negative	Trisomy 18 (T18)	Positive	Trisomy 13 (T13)	Negative	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Consistent with a male fetus.</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; font-size: 2em;">♂</td> </tr> </tbody> </table>	Consistent with a male fetus.	♂	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Fetal Fraction</th> <th>Sufficient</th> </tr> </thead> <tbody> <tr> <td>Number of Fetuses</td> <td>1</td> </tr> <tr> <th colspan="2">Gestational Age</th> </tr> <tr> <td>Weeks</td> <td>15</td> </tr> <tr> <td>Days</td> <td>1</td> </tr> </tbody> </table>	Fetal Fraction	Sufficient	Number of Fetuses	1	Gestational Age		Weeks	15	Days	1
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**Additional Chromosome Results**

Chromosome Tested	Results	Interpretation
Sex Chromosomes	No aneuploidy	No apparent abnormality was detected. See "Limitations" below.
Microdeletions	Not detected	No apparent abnormality was detected. See "Limitations" below.

**Laboratory Comments**

n/a

**Clinician Provided High-Risk Indications**

Component	Response	Component	Response
Advanced Maternal Age	Yes	Abnormal Ultrasound	No
Abnormal Maternal Serum Screening	No	Personal/Family History	No

Healthcare providers: please contact your local Quest Diagnostics genetic counselor or call 866-GENEINFO (866-436-3463) for assistance with interpretation of these results.

**Limitations**

The test has been validated on women with a singleton pregnancy that is >>10 weeks' gestational age, and has limited data available for performance in multiple gestation pregnancy. Specimens are analyzed for aneuploidy of chromosomes 21, 18, 13, X, Y and microdeletion regions of interest only. Abnormalities of other chromosomes or those involving only a portion of chromosome outside the regions of interest cannot be excluded. DNA test results do not provide a definitive genetic risk in all individuals. Circulating cell-free fetal DNA does not replace the accuracy and precision of prenatal diagnosis with CVS or amniocentesis. A negative test result does not ensure an unaffected pregnancy. While the results of this test are highly accurate, not all chromosome abnormalities may be detected due to placental, maternal, or fetal mosaicism, or other causes. Sex chromosome aneuploidy is not reportable for known multiple gestation pregnancies. The healthcare provider is responsible for the use of this information in the management of his/her patient. Healthcare providers, please contact your local Quest Diagnostics genetic counselor or call 866-GENEINFO (866-436-3463) for assistance with interpretation of these results.

CLIENT SERVICES: 866.697.8378      SPECIMEN: SL006083J      PAGE 1 OF 2

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## For your reference: general overview of select microdeletions

Name	Site of Anomaly	Frequency of Live Births	Description
<b>DiGeorge Syndrome</b>	22q11	1 in 4,000	DiGeorge syndrome (also known as CATCH22) is an autosomal dominant condition caused by a small deletion on the long arm of chromosome 22. The disorder is characterized by cardiac abnormalities, abnormal facies, thymic aplasia, cleft palate, hypocalcemia and schizophrenia. Most cases are not inherited (de novo) but transmission from a parent carrying the 22q11 deletion is seen in about 10% of cases. <a href="http://ghr.nlm.nih.gov/condition/22q112-deletion-syndrome">http://ghr.nlm.nih.gov/condition/22q112-deletion-syndrome</a>
<b>1p36 Deletion Syndrome</b>	1p	1 in 10,000	1p36 deletion syndrome (monosomy 1p36 syndrome) is characterized by a deletion on the short arm of chromosome 1. The disorder is characterized by severe intellectual disability, dysmorphic craniofacial features, developmental delay, brain abnormalities, short feet, severe congenital heart defects, hypotonia, and brachy/camptodactyly. Most cases are not inherited (de novo) but transmission from an unaffected parent carrying a balanced translocation is seen in about 20% of cases. <a href="http://ghr.nlm.nih.gov/condition/1p36-deletion-syndrome">http://ghr.nlm.nih.gov/condition/1p36-deletion-syndrome</a>
<b>Angelman Syndrome and Prader-Willi Syndrome</b>	15q	1 in 20,000	Both Angelman (AS), a maternal deletion, and Prader-Willi (PWS), a paternal deletion, syndromes are caused by deletions on the long arm of chromosome 15. AS is associated with delayed development, intellectual disability, severe speech impairment, and problems with movement and balance. Most affected children have recurrent seizures and small head size. Delayed development becomes noticeable by the age of 6 to 12 months. PWS presents in infancy characterized by weak muscle tone, feeding difficulties, poor growth, and delayed development. In childhood, it is associated with an insatiable appetite. <a href="http://ghr.nlm.nih.gov/condition/angelman-syndrome">http://ghr.nlm.nih.gov/condition/angelman-syndrome</a> <a href="http://ghr.nlm.nih.gov/condition/prader-willi-syndrome">http://ghr.nlm.nih.gov/condition/prader-willi-syndrome</a>
<b>Cri-du-chat Syndrome</b>	5p	1 in 50,000	Cri-du-chat syndrome (5p minus) is caused by a partial deletion of the short arm of chromosome 5. The disorder is characterized by intellectual disability, developmental delay, microcephaly, hypotonia, distinctive facial features, heart defects, and a characteristic cat-like cry. Most cases are not inherited (de novo) but transmission from an unaffected parent carrying a balanced translocation is seen in about 10% of cases. <a href="http://ghr.nlm.nih.gov/condition/cri-du-chat-syndrome">http://ghr.nlm.nih.gov/condition/cri-du-chat-syndrome</a>
<b>Wolf-Hirschhorn Syndrome</b>	4p	1 in 50,000	Wolf-Hirschhorn syndrome is caused by a deletion on the short arm of chromosome 4. It is characterized by distinct facial appearance, delayed growth and development, intellectual disability, and seizures. Most cases are not inherited (de novo). <a href="http://ghr.nlm.nih.gov/condition/wolf-hirschhorn-syndrome">http://ghr.nlm.nih.gov/condition/wolf-hirschhorn-syndrome</a>
<b>Jacobsen Syndrome</b>	11q	1 in 100,000	Jacobsen syndrome is caused by a deletion on the long arm of chromosome 11. It is characterized by distinctive facial features, delayed development, including motor skills (such as sitting, standing and walking) and speech. Most also have cognitive impairment and learning difficulties. Behavioral problems have been reported including compulsive behavior (such as shredding paper), a short attention span, and easy distractibility. Many with Jacobsen syndrome have been diagnosed with attention deficit-hyperactivity disorder (ADHD). <a href="http://ghr.nlm.nih.gov/condition/jacobsen-syndrome">http://ghr.nlm.nih.gov/condition/jacobsen-syndrome</a>
<b>Langer-Giedion Syndrome</b>	8q	Rare	Langer-Giedion syndrome is caused by a deletion on the long arm of chromosome 8. It is characterized by benign bone tumors (exostoses), short stature, and distinctive facial features. Most cases are not inherited (de novo). Exostoses may result in pain, limited range of joint movement, and pressure on nerves, blood vessels, the spinal cord, and tissues surrounding the exostoses. <a href="http://ghr.nlm.nih.gov/condition/langer-giedion-syndrome">http://ghr.nlm.nih.gov/condition/langer-giedion-syndrome</a>





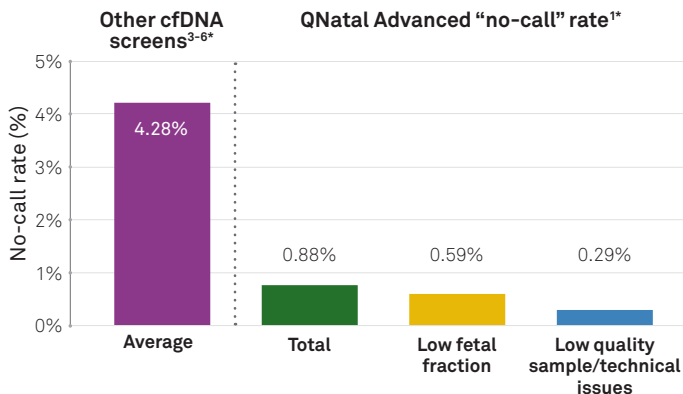
## Count on greater accuracy across a wide range of conditions

- Reports both common and rare fetal chromosomal abnormalities, from trisomies 21, 18 and 13 to fetal sex aneuploidies and microdeletion variants
- Appropriate for all pregnancies, including multiple gestations and IVF using donor eggs
- Test can be ordered as early as 10 weeks' gestation

## Expect clear results with a very low “no-call” rate

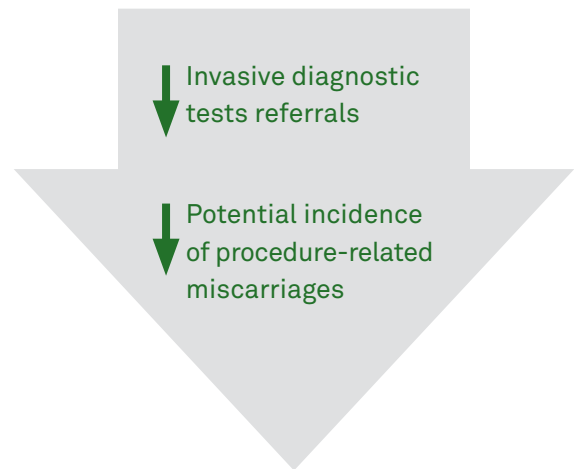
QNatal Advanced validated technology and advanced bioinformatics generate low nonreportable rates, so you and your patients can count on test accuracy and avoid retesting or unnecessary invasive procedures.

QNatal Advanced demonstrated an overall “no-call” rate of 0.88% in an analysis of the first 10,713 commercial samples<sup>1</sup>



\*No-call rates include suspected, borderline, and indeterminate samples

A reduction in the “no-call” rate may lead to<sup>7,8</sup>



Not all “no-call” rates are calculated or reported in the same manner. Ask what is or is not included when a “no-call” rate is given.

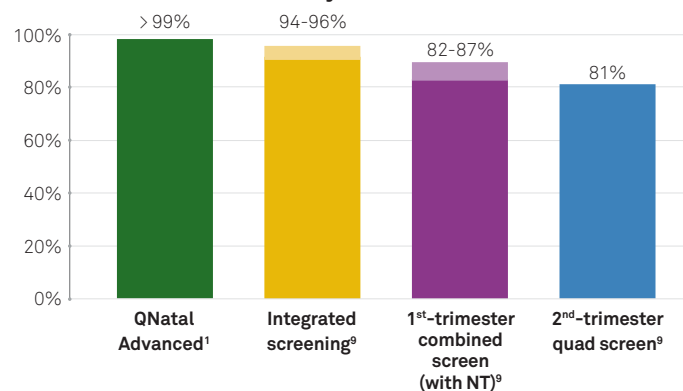
- Low fetal fraction
- Unmet quality metrics
- Uninformative DNA pattern
- Technical-related issues
- Sample-related issues
- Redraws
- Suspected/borderline results\*



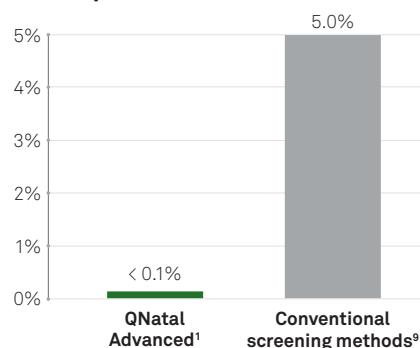
ACOG guidelines (Committee Opinion No.640, September 2015) recommend that women who receive a positive, or “no-call” or suspected/borderline test result from cfDNA prenatal screening should receive genetic counseling as well as be offered comprehensive ultrasound evaluation and diagnostic testing because of an increased risk of aneuploidy.<sup>8</sup>

## Noninvasive cfDNA screening is more accurate than traditional screening

### Detection Rate of Down Syndrome



### False-positive Rate



Test performed at:

≥ 10 weeks      11-13 weeks & 15-20 weeks      11-13 weeks      15-20 weeks

## Know more with the microdeletion option

QNatal Advanced microdeletion technology was validated using a genome-wide method examining de-identified blood specimens with karyotypic anomalies. The study was designed to test a selection of microdeletions/duplications ranging in size from 3 Mb to 40 Mb, not syndrome-specific microdeletions/duplications due to low prevalence rates.

QNatal Advanced provides excellent analytical performance across a wide dynamic range when screening for microdeletions/duplications, as shown below.

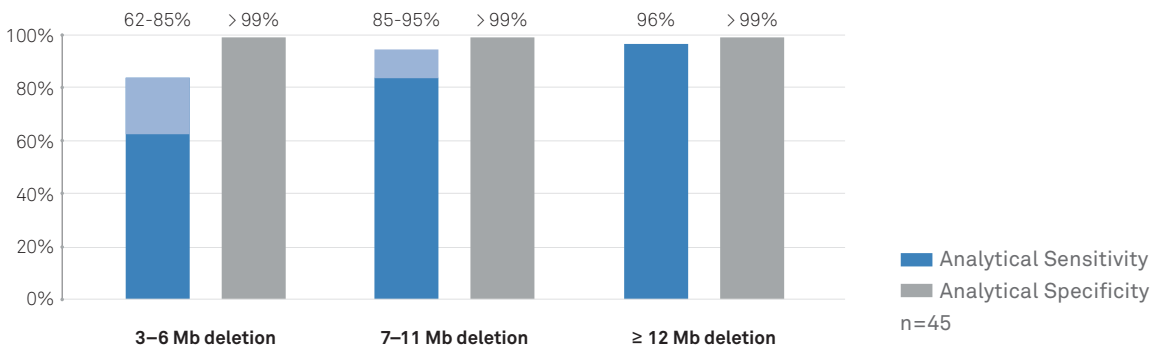
### Microdeletion Method Validation<sup>10</sup>

Microdeletion Detection	Rate	95% CI
Sensitivity	94.4% (17/18)	70.6-99.7%
Specificity	99.4% (156/157)	95.7-100.0%

### Microdeletion<sup>11-17</sup>

Genomic Region	Syndrome	Range of Deletion Size
1p36	1p36	1.5 to >10.5 Mb
8q24.11-q24.13	Langer-Giedion	1 to 25 Mb
4p16.3	Wolf-Hirschhorn	1.4 to 37 Mb
22q11.2	DiGeorge	1.5 to 3 Mb
15q11.2	Prader-Willi/Angelman	2 to 9 Mb
5p15.3	Cri-du-chat	3 to 32 Mb
11q23	Jacobsen	7 to 20 Mb

### Analytical performance based on size of abnormality<sup>10</sup>



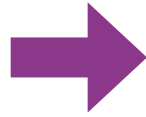
Note: Absence of an Additional Finding does not indicate a negative result. Analytical performance modeled on genomic DNA with plasma mixtures. Performance dependent on size of deletion, number of reads, fetal fraction, etc. Although deletions as small as 1.5 Mb have been detected, sensitivity in this range is variable due to size of the deletion.

## Quest Diagnostics is a leader in genetic testing

Quest Diagnostics provides a continuum of care for fetal aneuploidy testing by offering an extensive menu of first trimester screens as well as comprehensive diagnostic testing.

### Aneuploidy Screening

- First Trimester Screen
- Quad, Penta
- Integrated, Sequential
- QNatal™ Advanced



### Diagnostic Testing

- Amniocentesis
- CVS
  - Chromosomal microarray
  - Karyotyping
  - FISH

Test Name	Test Code	CPT Code*	Specimen Requirements
QNatal Advanced	92777(X)	81420	<ul style="list-style-type: none"> <li>• 20mL whole blood, minimum 16mL, collected in two Streck tubes (glass tubes with black and tan stopper)</li> <li>• Store specimens at room temperature; do not refrigerate or freeze</li> </ul>

\*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

For more information, contact your Quest Diagnostics sales representative or visit [QuestDiagnostics.com/NIPS](http://QuestDiagnostics.com/NIPS).

For clinician consultation on test results, contact **1.866.GENE.INFO (1.866.436.3463)**.

Note: No test is perfect. DNA test results do not provide a definite genetic risk in all individuals. Cell-free fetal DNA does not replace the accuracy and precision of prenatal diagnosis with CVS or amniocentesis. A patient with a positive test result or an Additional Finding should be referred for genetic counseling and offered invasive prenatal diagnosis for confirmation of test results. A negative test result does not ensure an unaffected pregnancy. The absence of an Additional Finding does not ensure an unaffected pregnancy. While results of this testing are highly accurate, not all chromosomal abnormalities may be detected due to placental, maternal or fetal mosaicism, or other causes. Sex chromosomal aneuploidies are not reportable for known multiple gestations. The healthcare provider is responsible for the use of this information in the management of their patient.

QNatal Advanced noninvasive prenatal screening is a laboratory-developed test, developed and performed exclusively by Quest Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Although laboratory-developed tests to date have not been subject to U.S. FDA regulation, certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. QNatal Advanced noninvasive prenatal screening is performed exclusively by Quest Diagnostics.

### References

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