ARUP
Non-Invasive Prenatal Testing for Fetal Aneuploidy
(powered by Constellation)

Information in this brochure is current as of October 2018. All content is subject to change. Please contact ARUP Client Services at (800) 522-2787 with any questions or concerns.

www.aruplab.com
ARUP offers non-invasive prenatal testing (NIPT) as early as 9 weeks gestation to help manage your patient’s pregnancy. Maternal blood is used to screen for specific chromosomal aneuploidies in the fetus, and results are reported as either low risk or high risk.

**Conditions screened:**
- Trisomy 21 (Down syndrome)
- Trisomy 18
- Trisomy 13
- Triploidy/vanishing twin
- Sex chromosome aneuploidies:
  - Monosomy X (Turner syndrome)
  - XXY (Klinefelter syndrome)
  - XXX
  - XYY

**Also included:**
- Fetal fraction (%)
- Fetal sex (patient may opt out)

Each patient report includes interpretive comments carefully drafted by ARUP medical directors and genetic counselors. As **NIPT is a screening test and is not diagnostic for the conditions reported**, any patient with a result indicating a potential abnormality should be offered confirmatory diagnostic testing via amniocentesis or CVS, or testing of the baby after delivery.1

**What is Constellation?**

ARUP’s NIPT uses Natera’s Constellation software to analyze copy numbers of chromosomal regions. Constellation is a cloud-based, general-purpose software that facilitates the interpretation of test data by ARUP’s medical directors and genetic counselors.

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For more information about NIPT, visit: [www.aruplab.com/NIPT](http://www.aruplab.com/NIPT)
Non-Invasive Prenatal Testing for Fetal Aneuploidy

Patient: DOCVAL, 1804
DOB: 04/04/1982  Age: 35  Gender: F

Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
Physician: VAL, NIPT

ARUP Test Code: 2007537
Collection Date: 01/30/2018
Received in lab: 01/30/2018
Completion Date: 01/30/2018

Patient Information Used in Risk Calculations
Maternal Age at Delivery: 36 years
Estimated Due Date: 19 Jun 2018
Gestational Age at Draw: 20 weeks 0 days
Maternal Weight: 150 lbs
Report Fetal Sex: Yes

Results Summary
HIGH RISK Trisomy 21
Fetal Fraction: 8.0%  Fetal Sex: Female
This pregnancy is classified as HIGH RISK for trisomy 21 (Down syndrome) by this screen. This result should be confirmed by a diagnostic test. On average, 91% of pregnancies classified as HIGH RISK are found to have trisomy 21 based on a published study of 17,885 women (PMID 25111587).
This is a screening test, and is NOT diagnostic for the conditions listed in this report. Both false positive and false negative results may occur. Genetic counseling and confirmatory fetal diagnostic testing is recommended. Irrevocable action such as pregnancy termination should not be taken based on the results of this test alone.
This result has been reviewed and approved by Electronic Signature

Conditions Screened
Trisomy 21: HIGH RISK
Trisomy 18: Low risk
Trisomy 13: Low risk
Monosomy X: Low risk
Triploidy/Vanishing twin: Low risk

example only
Performance of NIPT

The performance of ARUP's NIPT is very similar to Natera's NIPT. It has the ability to distinguish between fetal and maternal DNA in the mother's blood and detects aneuploidies in fetal fractions as low as 2.8 percent. A blinded study proved its strong performance in the detection of aneuploidy and fetal sex determination.2

<table>
<thead>
<tr>
<th>ARUP Validation Data</th>
<th>Agreement with Natera, Inc., Panorama</th>
<th>Concordance with Clinical Outcome</th>
<th>PPV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk (negative)</td>
<td>100% (146/146)</td>
<td>98.3% (58/59)**</td>
<td>NA</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>100% (18/18)</td>
<td>&gt; 99% (11/11)</td>
<td>91%³</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>100% (9/9)</td>
<td>&gt; 99% (3/3)</td>
<td>93%³</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>100% (5/5)</td>
<td>&gt; 99% (1/1)</td>
<td>38%³</td>
</tr>
<tr>
<td>Monosomy X</td>
<td>100% (8/8)</td>
<td>&gt; 99% (1/1)</td>
<td>50%³</td>
</tr>
<tr>
<td>Sex chromosome trisomy: XXX, XXY, XYY</td>
<td>100% (11/11)</td>
<td>NA (0/0)</td>
<td>54% (XXX)⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>63% (XXY)⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>88% (XYY)⁴</td>
</tr>
<tr>
<td>Triploidy or twin</td>
<td>100% (4/4)</td>
<td>&gt; 99% (9/9)</td>
<td>No data</td>
</tr>
<tr>
<td>Fetal sex</td>
<td>100% (99/99)</td>
<td>&gt; 99% (73/73)</td>
<td>100%³</td>
</tr>
</tbody>
</table>

* PPV (positive predictive value) indicates the percentage of pregnancies classified as high risk by NIPT that were found to actually have the aneuploidy based on published or internal data.

** One sample, 46,XY (normal male) by karyotype on amniocytes, exhibited a distinct pattern of XXY, suggesting a possible difference between placental DNA found in plasma and the actual fetal DNA. Independent review by Natera also called this case XXY.
A small, missing ("deleted") piece of a chromosome is called a microdeletion. Unlike aneuploidies, such as Down syndrome, which occur more frequently in older mothers, microdeletions can occur in pregnancies of younger mothers at the same rate as they do in older mothers. As a group, they happen in a random fashion at a frequency of one in 1,000 pregnancies.

Five microdeletions, all of which can be associated with serious health issues, can be screened for (in addition to aneuploidies in the basic NIPT screen).

- 22q11.2 deletion syndrome/DiGeorge syndrome
- Prader-Willi syndrome
- Angelman syndrome
- 1p36 deletion syndrome
- Cri-du-chat syndrome

Screening for aneuploidies (T21, T18, T13, MX), and fetal sex will always be performed in addition to microdeletions.

<table>
<thead>
<tr>
<th></th>
<th>Agreement with Natera</th>
<th>Concordance with Clinical Outcome</th>
<th>PPV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined Microdeletions</td>
<td>&gt;99% (981/984)</td>
<td>95% (38/40)</td>
<td>40%</td>
</tr>
<tr>
<td>DiGeorge (22q11.2)</td>
<td>&gt;99% (244/246)</td>
<td>&gt;90% (10/10)</td>
<td>20%</td>
</tr>
<tr>
<td>Prader-Willi/Angelman</td>
<td>&gt;99% (245/246)</td>
<td>90% (9/10)</td>
<td>4—5%</td>
</tr>
<tr>
<td>1p36d</td>
<td>100% (246/246)</td>
<td>90% (9/10)</td>
<td>17%</td>
</tr>
<tr>
<td>Cri-du-chat (5p-)</td>
<td>100% (246/246)</td>
<td>&gt;90% (10/10)</td>
<td>5%</td>
</tr>
</tbody>
</table>

For more information about NIPT, visit: www.aruplab.com/NIPT
Non-Invasive Prenatal Testing for Fetal Aneuploidy with Microdeletions

2010232 Non-Invasive Prenatal Testing for Fetal Aneuploidy with Microdeletions
2013142 Non-Invasive Prenatal Testing for Fetal Aneuploidy with 22q11.2 Microdeletion

### Non-Invasive Prenatal Testing for Fetal Aneuploidy with Microdeletions

**Patient Information Used in Risk Calculations**
- **Maternal Age at Delivery:** 36 years
- **Estimated Due Date:** 19 June 2016
- **Gestational Age at Draw:** 20 weeks 0 days

**Results Summary**

**HIGH RISK** 1p36 deletion syndrome

- **Fetal Fraction:** 10.3%
- **Fetal Sex:** Male

This pregnancy is classified as HIGH RISK by this screen for a deletion at 1p36, which is associated with 1p36 deletion syndrome. This result should be confirmed by a diagnostic test. Dependent on fetal fraction, 7 to 17% of pregnancies classified as HIGH RISK are found to have 1p36 deletion syndromes.

This is a screening test, and is NOT diagnostic for the conditions listed in this report. Both false positive and false negative results may occur. Genetic counseling and confirmatory fetal diagnostic testing, including SNP microarray, is recommended. Irreversible action such as pregnancy termination should not be taken based on the results of this test alone.

This result has been reviewed and approved by

**PH.D., FACMG**

**Electronic Signature**

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<thead>
<tr>
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<th>Trisomy 21</th>
<th>Low risk</th>
<th>1p36 deletion syndrome</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 18</td>
<td>Low risk</td>
<td>Patau syndrome</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>Low risk</td>
<td>Angelman syndrome</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Monosomy X</td>
<td>Low risk</td>
<td>Cri-du-chat syndrome</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Triploidy/Vanishing twin</td>
<td>Low risk</td>
<td>triplicletion syndrome</td>
<td>HIGH RISK</td>
<td></td>
</tr>
</tbody>
</table>

### Non-Invasive Prenatal Testing for Fetal Aneuploidy with 22q11.2 Microdeletion

**Patient Information Used in Risk Calculations**
- **Maternal Age at Delivery:** 36 years
- **Estimated Due Date:** 19 June 2016
- **Gestational Age at Draw:** 20 weeks 0 days

**Results Summary**

**HIGH RISK** 22q11.2 deletion syndrome

- **Fetal Fraction:** 10.3%
- **Fetal Sex:** Male

This pregnancy is classified as HIGH RISK by this screen for a deletion at 22q11.2, which is associated with 22q11.2 deletion syndrome. This result should be confirmed by a diagnostic test. 7 to 17% of pregnancies classified as HIGH RISK are found to have 22q11.2 deletion syndromes.

This is a screening test, and is NOT diagnostic for the conditions listed in this report. Both false positive and false negative results may occur. Genetic counseling and confirmatory fetal diagnostic testing, including SNP microarray, is recommended. Irreversible action such as pregnancy termination should not be taken based on the results of this test alone.

This result has been reviewed and approved by

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<td>Low risk</td>
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<td>Low risk</td>
<td></td>
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<td>Triploidy/Vanishing twin</td>
<td>Low risk</td>
<td>triplicletion syndrome</td>
<td>HIGH RISK</td>
<td></td>
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</tbody>
</table>
References


2. ARUP whitepaper. Noninvasive prenatal testing for fetal aneuploidy, powered by Natera’s Constellation. Results current as of November 2016.


4. ARUP historical data.


7. Kalyan A, et al. Performance of a SNP-based NIPT in screening for five clinically significant microdeletions in a large clinical cohort. International Society for Prenatal Diagnosis (ISPD). 20th International Conference on Prenatal Diagnosis and Therapy. July 10–13, 2016. Berlin, Germany [meeting abstract P-192]. The overall PPV listed here is from the latest data in which the PPV for the individual regions were higher than listed in this table.