ARUP LABORATORIES | NATIONAL REFERENCE LABORATORY

A nonprofit enterprise of the University of Utah and its Department of Pathology

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INFORMED CONSENT FOR NON-INVASIVE PRENATAL TESTING (NIPT)

NIPT is a screening test which can be performed on women at or after 9 weeks 0 days gestation, primarily to identify fetuses at risk to have extra or missing copies of chromosomes 13, 18, 21, X or Y. **This test is not intended to diagnose these conditions, and additional tests are recommended to confirm any positive NIPT results.**

NIPT will identify most fetuses with the following chromosomal conditions. Please see the table below for information regarding which test screen for which disorders:

- Trisomy 21 (T21) – is commonly known as Down syndrome and is caused by an extra copy of chromosome 21
- Trisomy 18 (T18) - is caused by an extra copy of chromosome 18 and is sometimes referred to as "Edwards syndrome"
- Trisomy 13 (T13) - is occasionally called "Patau syndrome" and is caused by an extra copy of chromosome 13
- Turner syndrome (45,X) – is also known as monosomy X and is usually caused by a missing sex chromosome (either X or Y)
- Triploidy (69,XXX/69,XXY/69,XYY) - is caused by an extra copy of each chromosome
- 22q11.2 deletion syndrome -- caused by the loss of a small piece of chromosome 22 that results in overlapping phenotypes known as DiGeorge and Velocardiofacial (VCFS) syndromes
- 1p36 deletion syndrome -- caused by loss of a small piece of the short arm of chromosome 1
- Angelman syndrome – usually caused by a deletion of a small piece of the chromosome 15 inherited from the mother of the fetus
- Prader-Willi syndrome – usually caused by a deletion of a small piece of the chromosome 15 inherited from the father of the fetus
- 5p deletion syndrome (*cri-du-chat*) -- caused by the loss of a small piece of the short arm of chromosome 5

Other conditions which may be detected and reported include sex chromosome trisomies such as 47,XXY (Klinefelter syndrome), 47,XYY and 47,XXX

Please note that under very few circumstances is a woman at increased risk to have a baby with a microdeletion. Therefore, all women should be considered *low-risk* to have a child with a microdeletion, and pretest genetic counseling should be considered to help women fully understand the benefits and limitations of microdeletion screening.

Test* / Disorder	Non-Invasive Prenatal Testing for Fetal Aneuploidy	Non-Invasive Prenatal Testing for Fetal Aneuploidy with 22q11.2 Microdeletion	Non-Invasive Prenatal Testing for Fetal Aneuploidy with Microdeletions
Trisomy 21	✓	✓	✓
Trisomy 18	✓	✓	✓
Trisomy 13	✓	✓	✓
Monosomy X	✓	✓	✓
Sex chromosome trisomies	✓	✓	✓
Triploidy	✓	✓	✓
22q11.2 deletion		✓	✓
1p36 deletion			✓
Angelman syndrome			✓
Prader-Willi syndrome			✓
5p deletion			✓
Twin, Egg donor, or surrogate pregnancies**	✓	✓†	

*Specimens received from New York will be performed at Natera until further notice.
**Testing ordered on twins, egg donor or surrogate pregnancies will be performed at Natera.
†Available for monozygotic twins only

There are four possible test results:

1. A "High Risk" result indicates that the screen has detected a significantly increased risk for the fetus to have an abnormal number of one of the following chromosomes: 13, 18, 21, X or Y, or a deletion at one of the specified genomic locations. The positive predictive value (chance the fetus is affected) for the specific disorder will be included in the report. Patients with a high risk NIPT result should be referred for genetic counseling and offered diagnostic testing.
2. A "Low Risk" result means the screen detected a very low chance (less than 1 in 100) for the fetus to have an abnormal number of any of the above chromosomes or a deletion at one of the specified genomic locations. However, your healthcare provider may still recommend a fetal karyotype or other testing if your fetus is found to have ultrasound anomalies or there are other concerns about your fetus' health.
3. A "No Result" occurs when the lab is unable to interpret the results of the screen. This may be due to too little fetal DNA (low fetal-

fraction); a low level of total cell-free DNA present in the maternal sample; mosaicism in the fetus, placenta, or mother; if the patient is not the genetic mother of the fetus; or may also occur if the mother and the father of the fetus are related by blood (e.g. cousins). Under some circumstances, the laboratory may request a second sample (at no charge) to clarify the test results.

4. A result of "Unchanged" is possible for microdeletions only. This indicates that the screen was unable to determine if your risk to have a child with the deletion was either increased or decreased. The population risk will be reported in these cases. A repeat screen is not indicated.

The following has been explained to me:

1. NIPT is a highly accurate screening test, but is not intended to replace diagnostic testing by CVS or amniocentesis. These tests are available to me.
2. This test has the ability to identify fetal sex.
   a) Fetal sex will be reported unless the "No" box is checked on the patient history form.
   b) If the fetus is at high risk to have Turner syndrome, XXX, XXY, or XYY, that result will be reported to me, even if I have elected not to have fetal sex disclosed.
3. NIPT may:
   a) indicate that my fetus is at increased risk to have one or more specific chromosome abnormalities (Down syndrome, Trisomy 18, Trisomy 13, Turner syndrome, triploidy, or a sex chromosome trisomy);
   b) be indeterminate due to biological or technical limitations;
   c) suggest a biological relationship between the mother and father of the fetus;
   d) identify a chromosomal abnormality in the mother of the fetus.
4. Limitations of NIPT include:
   a) **This is a screening test, not a diagnostic test. False positive and false negative results may occur. Positive results should be confirmed by direct fetal testing**.
   b) Testing is limited to the chromosomes and conditions listed above. This test will not identify other abnormalities of the tested chromosomes such as deletions or duplications, and does not detect abnormalities of chromosomes other than those tested.
   c) Balanced chromosomal rearrangements such as translocations or inversions, other genetic disorders, birth defects, and other fetal or pregnancy complications will not be detected.
   d) Results may not be interpretable if there is too little fetal DNA present in the sample (low fetal fraction). In these cases, a repeat test at no extra laboratory charge will be offered.
      - High maternal BMI is a common reason for low fetal fraction. In the case of maternal obesity, performing testing after 14 weeks gestation may increase the likelihood of obtaining results.
   e) Mosaic (the presence of both normal and abnormal cells) aneuploidy for the targeted chromosomes may not be detected.
   f) Aneuploidy screening can be performed using this method in twin gestations, or if the patient whose blood is being tested is not the genetic mother of the fetus (i.e. if the fetus was conceived using another woman's egg). However, testing cannot be performed if more than one of these conditions is true (i.e. cannot be performed if the patient used an egg donor AND is carrying twins).
   g) Triploidy cannot be distinguished from a vanishing or existing twin gestation. Ultrasound and/or direct fetal testing may be necessary to distinguish between these two possibilities. Triploidy will not be reported in stated twin or egg donor pregnancies.
5. A "high risk" result greatly increases the chances that the fetus has an extra copy of any of the tested chromosomes, or has a deletion of one of the targeted microdeletion sites, but false positive test results do occur. Thus, **positive results should be confirmed by direct fetal testing.**
6. A "low risk" result greatly reduces the chances that the fetus has an extra copy of any of the tested chromosomes, or has a deletion of one of the targeted microdeletion sites, but false negative test results can occur. If clinical results contradict test results, then diagnostic fetal testing (CVS or amniocentesis) should be considered.
7. Several sources of error are possible including, but not limited to: sample mishandling, sample misidentification, and sample contamination.
8. Residual DNA samples may be stored indefinitely to be used for test validation or education after personal identifiers are removed. Samples from New York clients, however, will be disposed of 60 days after testing is complete. No clinical tests other than those authorized will be performed. I may request disposal of my blood and DNA sample following completion of the test requested above by contacting the laboratory at (800) 242-2787, ext. 3301. Refusal to permit the use of my sample for test validation or education will not affect my test result. For more information about ARUP, please refer to www.aruplab.com.

The performance characteristics these tests were validated by ARUP Laboratories and Natera. The U.S. Food and Drug Administration (FDA) has not approved this test; however, FDA approval is currently not required for clinical use of this test. ARUP and Natera are authorized under Clinical Laboratory Improvement Amendments (CLIA) and by all states to perform high-complexity testing. These results are not intended to be used as the sole means for clinical diagnosis or patient management decisions.

NIPT is a fee-for-service test. I will be responsible for payment after the testing has begun, even if I decide not to receive results. ARUP will provide a local referral for genetic counseling at my request.

PATIENT CONSENT STATEMENT

I have read or have had read to me the above informed consent information about the Non-Invasive Prenatal Test (NIPT). I have had the opportunity to ask questions of my health care provider regarding this test, the risks, and the alternatives prior to my informed consent. I request and authorize ARUP to test my sample(s) for the fetal chromosome conditions listed above.

Patient/Guardian Signature _____ Date _____

PHYSICIAN/GENETIC COUNSELOR

I have explained NIPT and its limitations to the patient or legal guardian and answered all questions.

Printed Name of Provider: _____ Date _____

Signature _____ Phone Number _____