Patient Information

Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	123233-2-N
Reference ID:	254233-2-N
Accessioning ID:	C47695
Case File ID:	-159466

Test Information

Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

panorama® natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
LOW RISK	**Male**	**8.3%**

Notes by the clinical reviewer, if any, will be shown here.

RESULT DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[3]
Trisomy 21	Low Risk	1/152	<1/10,000
Trisomy 18	Low Risk	1/354	<1/10,000
Trisomy 13	Low Risk	1/1,116	<1/10,000
Monosomy X	Low Risk	1/255	<1/10,000
Triploidy	Low Risk		

RESULT DETAILS: MICRODELETIONS

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[4]
22q11.2 deletion syndrome	Low Risk	1/2,000	1/9,000

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Risk after test for aneuploidy incorporates results from the Panorama algorithm and data from a published population study of over 1 million women [DiNonno et al.J.Clin.Med.2019.Aug 26; 8(9):1311.doi:10.3390/jcm8091311] and are reported as PPVs (high risk) and NPVs (low risk). Maternal age and fetal fraction are utilized in this calculation; however, the "risk after test" may not reflect the actual PPVs for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, and personal/family history, are not included in the risk assessment. 4. Risk after test for microdeletion(s) incorporates results from the Panorama algorithm and data from multiple studies [Dar et al. Society for Maternal Fetal Medicine 41st Annual Pregnancy Meeting; January 25-30, 2021.; Martin et al. Clin Genetics. 2017 Jul 11, Wapner R J et al. Am J Obstst Gynecol. 2015 Mar;212 (3):332 .e1-9] and are reported as PPVs (high risk) and NPVs (low risk). Risks for microdeletions are independent of maternal age and fetal fraction is utilized in this calculation; however, the "risk after test" may not reflect the actual PPV for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, personal/family history, are not included in the risk assessment.

Reviewed By: Wenbo Xu, M.D., Ph.D., FACMG, Senior Laboratory Director

CLIA Laboratory Director: J. Dianne Keen-Kim, Ph.D., FACMG

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 650-249-9090 #3. Ask for the NIPT genetic counselor on call.

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panorama® natera prenatal screen

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OVERALL TEST SPECIFICATIONS FOR PANORAMA

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value (PPV) is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 95% chance that the fetus is affected by Trisomy 21. In other words, 5% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value (NPV) is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*PPV*	*NPV*
Trisomy 21 [1,2,3,4]	>99% (CI 97.8-99.9)	>99% (CI 99.7-100)	95%	>99.99%*
Trisomy 18 [1,2,3,4]	98.2% (CI 90.4-99.9)	>99% (CI 99.7-100)	91%	>99.99%*
Trisomy 13 [1,2,3,4]	>99% (CI 87.2-100)	>99% (CI 99.8-100)	68%	>99.99%*
Monosomy X [1,2,3,4]	94.7% (CI 74.0-99.9)	>99% (CI 99.7-100)	78%	>99.99%*
Triploidy [5,6]	>99% (CI 66.4-100)	>99% (CI 99.5-100)	5.3%	>99.99%*
XXX, XXY, XYY [7] **	73.1% (CI 61.0-85.1)	99.9% (CI 99.90-99.99)	86.4%	99.87%
22q11.2 deletion syndrome [8,9,10]	90.0% (CI 55.5-99.7)	>99% (CI 98.6-99.9)	53%***	99.97-99.99%****
Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		

1. Nicolaides KH et al. Prenat Diagn. 2013 June;33(6):575-9
2. Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8
3. Ryan A et al. Fetal Diagn Ther. 2016;40(3):219-223
4. DiNonno et al.J.Clin.Med.2019.Aug 26; 8(9):1311.doi:10.3390/jcm8091311
5. Nicolaides KH et al. Fetal Diagn Ther. 2014;35(3):212-7.
6. Curnow KJ et al. Am J Obstet Gynecol. 2015 Jan;212(1):79.e1-9
7. Martin K et al. 25th International Conference on Prenatal Diagnosis and Therapy Meeting; June 6-8, 2021
8. Martin et al. Clin Genetics. 2017 Jul 11
9. Norvez A et al. The European Human Genetics Conference, ESHG. Copenhagen, Denmark. May 27–30, 2017.
10. Dar et al. Society for Maternal Fetal Medicine 41st Annual Pregnancy Meeting; January 25–30, 2021

* Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.

** Sex chromosome abnormalities are only reported when identified.

*** PPV for 22q11.2 deletion syndrome and Angelman syndrome in published studies was 53% and 10% respectively when no ultrasound anomalies were seen and was up to 100% when ultrasound anomalies were seen prior to testing.

**** Dependent upon fetal fraction. For 22q11.2 deletion syndrome, only the paternal allele is evaluated at FF ≤ 6.5%. For 1p36 deletion syndrome and Cri-du-chat syndrome, only the paternal allele is evaluated at FF < 7%. For Angelman syndrome, no risk assessment is reported at FF < 7%. For Prader-Willi syndrome, no risk assessment is reported at FF ≤ 2.8%.

Test specifications above are applicable to singleton and monozygotic twin pregnancies only. For additional information, please visit: ***www.natera.com/panorama-test/test-specs***

Testing Methodology: DNA isolated from the maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay and is sequenced using a high-throughput sequencer. Fetal fraction is determined using a proprietary algorithm incorporating data from single nucleotide polymorphism-based (SNP-based) next-generation sequencing [Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8]. If the estimated fetal fraction is ≥2.8%, sequencing data is analyzed using a proprietary SNP-based algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X and Y [Ryan A et al. Am J Obstet Gynecol. 2014 Nov;211(5):527.e1-527.e17]. If ordered, specific microdeletions will be evaluated using similar methodology [Wapner RJ et al. Am J Obstet Gynecol. 2015 Mar;212(3):332.e1-9]. If a sample fails to meet the quality threshold, or the fetal fraction is insufficient, an additional algorithm is utilized to determine whether there is an increased risk for triploidy, trisomy 18 and trisomy 13 [McKanna et al. The European Human Genetics Conference. Copenhagen, Denmark. May 27-30, 2017]. However, some samples will not produce a result due to failure to meet the necessary quality thresholds.

This test has been validated on women with a singleton, twin or egg donor pregnancy of at least nine weeks gestation. A result will not be available for higher order multiples and multiple gestation pregnancies with an egg donor or surrogate, or bone marrow transplant recipients. Complete test panel is not available for twin gestations and pregnancies achieved with an egg donor or surrogate. For twin pregnancies with a fetal fraction value below the threshold for analysis, a sum of the fetal fractions for both twins will be reported. Findings of unknown significance will not be reported. As this assay is a screening test and not diagnostic, false positives and false negatives can occur. High risk test results need diagnostic confirmation by alternative testing methods. Low risk results do not fully exclude the diagnosis of any of the syndromes nor do they exclude the possibility of other chromosomal abnormalities or birth defects, which are not a part of this test. Potential sources of inaccurate results include, but are not limited to, mosaicism, low fetal fraction, limitations of current diagnostic techniques, or misidentification of samples. This test will not identify all deletions associated with each microdeletion syndrome. This test has been validated on full region deletions only and may be unable to detect smaller deletions. Microdeletion risk score is dependent upon fetal fraction, as deletions on the maternally inherited copy are difficult to identify at lower fetal fractions. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate.

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Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
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	Mother Blood

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PARTIAL RESULTS SUMMARY:

ANEUPLOIDIES AND MICRODELETIONS

Result
LOW RISK

Fetal Sex
Male

Fetal Fraction(s)
8.3%

Microdeletion results pending.

Notes by the clinical reviewer, if any, will be shown here.

FETAL RHD

Result
Fetal status not assessed

The pregnant patient is RHD negative by genotype due to the presence of the RHD pseudogene and therefore, the fetal status is not assessed.
Clinical management should be based upon the pregnant patient's Rh blood type result by routine serology. A repeat specimen is not indicated.

RESULT DETAILS: ANEUPLOIDIES

Condition Tested [1]	*Result*	*Risk Before Test* [2]	*Risk After Test* [3]
Trisomy 21	Low Risk	1/152	<1/10,000
Trisomy 18	Low Risk	1/354	<1/10,000
Trisomy 13	Low Risk	1/1,116	<1/10,000
Monosomy X	Low Risk	1/255	<1/10,000
Triploidy	Low Risk		

RESULT DETAILS: MICRODELETIONS

Condition Tested [1]	*Result*	*Risk Before Test* [2]	*Risk After Test* [4]
22q11.2 deletion syndrome	Pending	1/2,000	N/A
1p36 deletion syndrome	Pending	1/5,000	N/A
Angelman syndrome	Pending	1/12,000	N/A
Cri-du-chat syndrome	Pending	1/20,000	N/A
Prader-Willi syndrome	Pending	1/10,000	N/A

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Risk after test for aneuploidy incorporates results from the Panorama algorithm and data from a published population study of over 1 million women [DiNonno et al.J.Clin.Med.2019.Aug 26; 8(9):1311.doi:10.3390/jcm8091311] and are reported as PPVs (high risk) and NPVs (low risk). Maternal age and fetal fraction are utilized in this calculation; however, the "risk after test" may not reflect the actual PPVs for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, and personal/family history, are not included in the risk assessment. 4. Risk after test for microdeletion(s) incorporates results from the Panorama algorithm and data from multiple studies [Dar P et al. Cell-free DNA screening for prenatal detection of 22q11.2 deletion syndrome, American Journal of Obstetrics and Gynecology (2022), https://doi.org/10.1016/j.ajog.2022.01.002; Martin et al. Clin Genetics. 2017 Jul 11, Wapner R J et al. Am J Obstst Gynecol. 2015 Mar;212 (3):332 .e1-9] and are reported as PPVs (high risk) and NPVs (low risk). Risks for microdeletions are independent of maternal age and fetal fraction is utilized in this calculation; however, the "risk after test" may not reflect the actual PPV for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, personal/family history, are not included in the risk assessment.

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Testing Methodology: DNA isolated from maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay and is sequenced using a high-throughput sequencer. Fetal fraction is determined using a proprietary algorithm incorporating data from single nucleotide polymorphism-based (SNP-based) next-generation sequencing [Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8]. If there is sufficient fetal fraction, sequencing data is analyzed using a proprietary SNP-based algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X and Y. If ordered, specific microdeletions will be evaluated using similar methodology [Wapner RJ et al. Am J Obstet Gynecol. 2015 Mar;212(3):332.e1-9]. If the fetal fraction is insufficient, an additional algorithm to determine whether there is an increased risk for triploidy, trisomy 18, and trisomy 13 may be utilized, known as fetal fraction based risk assessment (FFBR) [McKanna et al. Ultrasound Obstet Gynecol 2019; 53:73-79]. If ordered, and pregnant patient is RhD negative by genotype, fetal RhD status will be evaluated using similar methodology if fetal fraction is sufficient [Wang et al. Detection of fetal RhD status on SNP-based prenatal cell-free DNA screening. In: American Society of Human Genetics; Nov 1-5, 2023; Washington, D.C.] However, some samples will not produce a result due to failure to meet the necessary quality thresholds.

This test has been validated on women with a singleton, twin or egg donor pregnancy of at least nine weeks gestation. A result will not be available for higher order multiples and multiple gestation pregnancies with an egg donor or surrogate, or bone marrow transplant recipients. Complete test panel is not available for twin gestations and pregnancies achieved with an egg donor or surrogate. For twin pregnancies with a fetal fraction value below the threshold for analysis, a sum of the fetal fractions for both twins will be reported. As this assay is a screening test and not diagnostic, false positives and false negatives can occur.

High risk aneuploidy and microdeletion test results need diagnostic confirmation by alternative testing methods. Low risk results do not fully exclude the diagnosis of any of the syndromes nor do they exclude the possibility of other chromosomal abnormalities or birth defects, which are not a part of this test. Potential sources of inaccurate results include, but are not limited to, mosaicism, low fetal fraction, limitations of current diagnostic techniques, or phlebotomy labeling errors. This test will not identify all deletions associated with each microdeletion syndrome. This test has been validated for deletions ≥0.5 Mb within the 22q11.2 A-D region. This test has been validated on full region deletions only for 1p36 deletion syndrome, Cri-du-chat syndrome, Prader Willi syndrome and Angelman syndrome and may be unable to detect smaller deletions. Microdeletion risk score may be dependent upon fetal fraction, as deletions on the maternally inherited copy are difficult to identify at lower fetal fractions. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate.

Fetal RhD non-invasive prenatal test does not replace the pregnant patient's serology result. False positive results may occur due to the presence of rare genotypes that include but are not limited to Weak D, Partial D, or RhD Pseudogene. False negative results, while rare, can also occur. Additional potential sources of inaccurate results include, but are not limited to, phlebotomy labeling errors, low fetal fraction, sample contamination, low DNA quantity, or low number of sequencing reads. Fetal RhD status will not be assessed for dizygotic twin pregnancies or in the context of certain maternal genetic variants. Test results should always be interpreted by a clinician in the context of clinical and familial data.

Reviewed By: Wenbo Xu, M.D., Ph.D., FACMG, Senior Laboratory Director

CLIA Laboratory Director: J. Dianne Keen-Kim, Ph.D., FACMG

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 844-778-4700, option 2. Ask for the NIPT genetic counselor on call.

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OVERALL TEST SPECIFICATIONS FOR PANORAMA

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value (PPV) is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 95% chance that the fetus is affected by Trisomy 21. In other words, 5% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value (NPV) is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*PPV*	*NPV*
Trisomy 21 [1.,1.]	99.0% (CI 97.1-100)	>99% (CI 99.93-99.99)	95%	>99.99%
Trisomy 18 [1.,1.]	94.1% (CI 82.9-100)	>99% (CI 99.96-100)	91%	>99.99%
Trisomy 13 [1.,1.]	>99% (CI 73.5-100)	>99% (CI 99.6-100)	68%	>99.99%
Monosomy X [1.,1.]	94.7% (CI 74.0-99.9)	>99% (CI 99.7-100)	78%	>99.99%
Triploidy [1.,1.]	>99% (CI 66.4-100)	>99% (CI 99.5-100)	7.5%	>99.99%
XXX, XXY, XYY [1.]	73.1% (CI 61.0-85.1)	99.9% (CI 99.90-99.99)	86.4%	99.87%
22q11.2 deletion syndrome [1.]	83.3% (CI 51.6-97.9)	>99% (CI 99.91-99.98)	53%	99.9% (CI 99.9-100)
1p36 deletion syndrome [1.,1.]	>99% (CI 2.5-100)	>99% (CI 99.1-100)	7-17%	99.98-99.99%
Angelman syndrome [1.,1.]	95.5% (CI 77.2-99.9)	>99% (CI 99.1-100)	10%	>99.99%
Cri-du-chat syndrome [1.,1.]	>99% (CI 85.8-100)	>99% (CI 99.1-100)	2-5%	>99.99%
Prader-Willi syndrome [1.,1.]	93.8% (CI 69.8-99.8)	>99% (CI 99.1-100)	5%	>99.99%
Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		
Fetal RhD+ [1.]	>99.9% (CI 98.9 - 100)	99.3% (CI 97.6 - 99.8)	99.4%	>99.99%

1. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.019
1. DiNonno W et al. J Clin Med. 2019. 26;8(9):1311. doi: https://doi.org/10.3390/jcm8091311
1. Martin et al. ISUOG World Congress 2022: September, 2022
1. Nicolaides KH et al. Fetal Diagn Ther. 2014. 35;(3):212-7. doi: https://doi.org/10.1159/000355655
1. Kantor et al. Prenat Diagn. 2022. 42;(8): 994-999. Doi: 10.1002/pd.6169
1. Martin K et al. ISPD 25th International Conference: June, 2021
1. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.002
1. Martin K et al. Clin Genet. 2018. 93(2):293-300. doi: https://doi.org/10.1111/cge.13098
1. Wapner RJ et al. Am J Obstet Gynecol. 2015. 212(3):332.e1-9. doi: https://doi.org/10.1016/j.ajog.2014.11.041
1. Natera internal validation data, 2024

Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.
Sex chromosome trisomies are only reported when clearly identified. At lower fetal fractions, identification of sex chromosome trisomies may not be possible.
Dependent upon fetal fraction. For 22q11.2 deletion syndrome, only the paternal allele is evaluated at FF ≤6.5%. For 1p36 deletion syndrome and Cri-du-chat syndrome, only the paternal allele is evaluated at FF <7%. For Angelman syndrome, no risk assessment is reported at FF<7%. For Prader-Willi syndrome, no risk assessment is reported at FF≤2.8%.

Test specifications above are applicable to singleton and monozygotic twin pregnancies only. For additional information, please visit: ***www.natera.com/panorama-test/test-specs***

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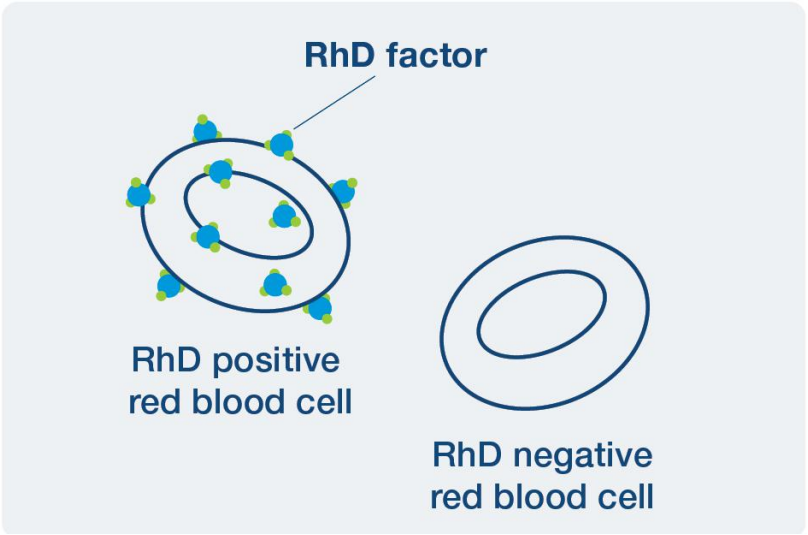
Understanding Your Results

Baby's predicted RhD factor not determined

What does this result mean?

This result means that your baby's RhD factor was not determined. There are two main reasons that a baby's RhD factor is not determined by this test. First, your own RhD factor could mean that it is not necessary to determine your baby's RhD factor. Second, sometimes the lab is not able to perform the test due to technical limitations.

What is RhD testing and why is it important in pregnancy?



RhD factor is a protein that can be present or absent on the surface of a person's red blood cells. RhD positive means that someone's red blood cells have the RhD protein on them. People who are RhD negative have red blood cells without this protein. The RhD factor can cause problems in a pregnancy if an RhD negative pregnant person's blood is mixed with RhD positive blood from the baby. When this happens, the RhD negative person's body will recognize the RhD factor on the RhD positive blood cells from the baby as foreign and will make antibodies to fight the RhD factor. When a pregnant person has RhD factor antibodies, they are said to be sensitized. If a sensitized pregnant person is carrying an RhD positive baby, the antibodies can cross the placenta and attack the baby's red blood cells. The antibodies can cause a loss of red blood cells, which can lead to serious health problems for the baby. When a pregnant person and their baby have different RhD factors, it is called RhD incompatibility.

Can I repeat this test to get an answer?

It depends on the reason that you did not get a result. Your lab report could say one of two things.

1. **Fetal status not assessed.** If your lab report says this, you should not repeat this test. You can get this result for one of two reasons.

    - "Fetal status not assessed" could mean that you are RhD positive. RhD incompatibility is not a risk to your baby if you are RhD positive.

    - Rarely, a result of "fetal status not assessed" could mean that you are RhD negative due to having what is called the *RHD* pseudogene. When a pregnant person has the *RHD* pseudogene, the lab does not determine the baby's RhD factor.

If your lab report says, "fetal status not assessed," please talk to your healthcare provider about looking at the results of other blood tests you had during pregnancy to determine what to do next.

2. **No results for fetal *RHD*.** If your lab report says this, the lab was not able to get a result. There are a few different reasons the lab would not be able to get a result. The reason you did not get a result is listed on your report. Sometimes this problem will not be solved by sending another blood sample. Many times the lab will be able to get a result on another sample. If another sample can be sent, your lab report will say so.

What should I do next?

Talk to your healthcare provider about next steps. Looking at the results of other blood tests you have had during pregnancy can sometimes help to explain this result. Sometimes your healthcare provider will recommend different blood tests, or it can sometimes be helpful to repeat this test. If you are RhD negative and it is important to know the baby's RhD factor, you could have the option of a test called CVS (chorionic villus sampling) or amniocentesis. These tests can tell you your baby's RhD factor. Both tests have a small risk of miscarriage.

Please talk to your healthcare provider about your result. If you would also like to discuss your result with a Natera genetic counselor, you can schedule a free information session at natera session.com, by texting* **SESSION** to **636363**, or by calling **1.877.467.4743**. Please select **Panorama non-invasive prenatal chromosome screening, post-test** as the appointment type.

You can find a local genetic counselor through the National Society of Genetic Counselors at findageneticcounselor.nsgc.org.

*Text scheduling is available only in the United States

13011 McCallen Pass, Building A Suite 100 | Austin, TX 78753 | natera.com

Patient Information

Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	254233-2-N
Accessioning ID:	C47695
Case File ID:	159466

Test Information

Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

panorama® natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

FINAL RESULTS SUMMARY: TWINS

Result	*Zygosity*	*Fetal Sex*	*Fetal Fraction(s)*
HIGH RISK for Monosomy X	**Monozygotic**	♀ **Female**	**8.3%**
	IDENTICAL TWINS	♀ **Female**	

This is a screening test only. Genetic counseling and diagnostic testing for both fetuses should be offered to further evaluate these findings.

Panorama analyzes DNA from the placenta. In some cases placental DNA can differ from that of the fetus; therefore, no irreversible decisions should be made based upon results of this screening test alone.

RESULT DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[3]
Trisomy 21	Low Risk	1/452	<1/10,000
Trisomy 18	Low Risk	1/1,054	<1/10,000
Trisomy 13	Low Risk	1/3,321	<1/10,000
Monosomy X	**High Risk**	**1/759**	**1/2**

RESULT DETAILS: MICRODELETIONS

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[4]
22q11.2 deletion syndrome	Low Risk	1/2,000	1/9,000

1. Reporting for Triploidy, 1p36 deletion syndrome, Angelman syndrome, Cri-du-chat syndrome and Prader-Willi syndrome is not available for monozygotic twin pregnancies. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Risk after test for aneuploidy incorporates results from the Panorama algorithm and data from a published study of 17,885 women [Dar et al. Am J Obstet Gynecol. 2014. Nov;211(5):527.e1-27.e17] and are reported as PPV (high risk) and NPV (low risk). Maternal age is utilized in this calculation, however the "risk after test" may not reflect the actual PPV for this patient, as additional risk factors, including but not limited to; results of other screening, ultrasound findings, personal/family history, are not included in the risk assessment. 4. Risk after test for microdeletion(s) incorporates results from the Panorama algorithm and data from published studies [Martin et al. Clin Genetics. 2017 Jul 11, Wapner R J et al. Am J Obstet Gynecol. 2015 Mar;212 (3):332 .e1-9] and are reported as PPV (high risk) and NPV (low risk). Risk for microdeletions is independent of maternal age. Fetal fraction (FF) is utilized in this calculation. Depending upon FF, in some cases only the paternal allele is evaluated (see page 2). The "risk after test" may not reflect the actual PPV for this patient, as additional risk factors, including but not limited to; results of other screening, ultrasound findings, personal/family history, are not included in the risk assessment.

Approved By: Susan Zneimer, Ph.D., FACMGG, Laboratory Director

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 650-249-9090 #3. Ask for the NIPT genetic counselor on call.

Patient Information

Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	254233-2-N
Accessioning ID:	C47695
Case File ID:	159466

Test Information

Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

panorama® natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

OVERALL TEST SPECIFICATIONS FOR PANORAMA

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 91% chance that the fetus is affected by Trisomy 21. In other words, 9% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*Positive Predictive Value*	*Negative Predictive Value*
Trisomy 21[1,2,3,4]	>99% (CI 97.8-99.9)	>99% (CI 99.7-100)	91%	>99.99%*
Trisomy 18[1,2,3,4]	98.2% (CI 90.4-99.9)	>99% (CI 99.7-100)	93%	>99.99%*
Trisomy 13[1,2,3,4]	>99% (CI 87.2-100)	>99% (CI 99.8-100)	38%	>99.99%*
Monosomy X[1,2,3,4]	94.7% (CI 74.0-99.9)	>99% (CI 99.7-100)	50%	>99.99%*
XXX, XXY, XYY[4]	N/A-Reported when identified	N/A-Reported when identified	89%	N/A-Reported when identified
22q11.2 deletion syndrome[5,6]	90.0% (CI 55.5-99.7)	>99% (CI 98.6-99.9)	20%**	99.97-99.99%***
Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		

1. Nicolaides KH et al. Prenat Diagn. 2013 June;33(6):575-9
2. Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8
3. Ryan A et al. Fetal Diagn Ther. 2016;40(3):219-223
4. Dar P et al. Am J Obstet Gynecol. 2014 Nov;211(5):527.e1-527.e17
5. Martin et al. Clin Genetics. 2017 Jul 11
6. Norvez A et al. The European Human Genetics Conference, ESHG. Copenhagen, Denmark. May 27–30, 2017.

* Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.

** PPV for 22q11.2 deletion syndrome and Angelman syndrome in published studies was 20% and 10% respectively when no ultrasound anomalies were seen and was up to 100% when ultrasound anomalies were seen prior to testing.

*** Dependent upon fetal fraction. For 22q11.2 deletion syndrome, only the paternal allele is evaluated at FF ≤ 6.5%. For 1p36 deletion syndrome and Cri-du-chat syndrome, only the paternal allele is evaluated at FF < 7%. For Angelman syndrome, no risk assessment is reported at FF < 7%. For Prader-Willi syndrome, no risk assessment is reported at FF ≤ 2.8%.

Test specifications above are applicable to singleton and monozygotic twin pregnancies only. For additional information, please visit: ***www.natera.com/panorama-test/test-specs***

Testing Methodology: DNA isolated from the maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay, and sequenced using a high-throughput sequencer. Sequencing data is analyzed using Natera's proprietary algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X, and Y, thereby identifying whole chromosome abnormalities at these locations, and if ordered, the microdeletion panel will identify microdeletions at the specified loci only. If a sample fails to meet the quality threshold, no result will be reported for the specified chromosome(s). The test requires sufficient fetal fraction to produce a result. Fetal fraction is determined using a proprietary algorithm incorporating data from single nucleotide polymorphism-based next-generation sequencing. Estimates of fetal fraction may differ when measured by different laboratories and/or methodologies.

Disclaimers: This test has been validated on women with a singleton, twin or egg donor pregnancy of at least nine weeks gestation. A result will not be available for higher order multiples and multiple gestation pregnancies with an egg donor or surrogate, or bone marrow transplant recipients. Complete test panel is not available for twin gestations and pregnancies achieved with an egg donor or surrogate. For twin pregnancies with a fetal fraction value below the threshold for analysis, a sum of the fetal fractions for both twins will be reported. Findings of unknown significance will not be reported. As this assay is a screening test and not diagnostic, false positives and false negatives can occur. High risk test results need diagnostic confirmation by alternative testing methods. Low risk results do not fully exclude the diagnosis of any of the syndromes nor do they exclude the possibility of other chromosomal abnormalities or birth defects, which are not a part of this test. Potential sources of inaccurate results include, but are not limited to, mosaicism, low fetal fraction, limitations of current diagnostic techniques, or misidentification of samples. This test will not identify all deletions associated with each microdeletion syndrome. This test has been validated on full region deletions only and may be unable to detect smaller deletions. Microdeletion risk score is dependent upon fetal fraction, as deletions on the maternally inherited copy are difficult to identify at lower fetal fractions. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate. The Panorama prenatal test was developed by Natera, Inc., a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA). This test has not been cleared or approved by the U.S, Food and Drug Administration (FDA).

Patient Information	
Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/ 0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	123233-2-N
Reference ID:	254233-2-N
Accessioning ID:	C47695
Case File ID:	-159466

Test Information	
Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

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FINAL RESULTS SUMMARY:

ANEUPLOIDIES AND MICRODELETIONS

Result
LOW RISK

Fetal Sex
Male

Fetal Fraction(s)
8.3%

Notes by the clinical reviewer, if any, will be shown here.

FETAL RHD

Result
Fetal status not assessed

The pregnant patient is RHD positive by genotype and therefore, the fetal status is not assessed. Reasons for this result type include Rh positive blood type or Rh negative blood type with Weak D, Partial D (e.g. DVI), or other rare RHD genotype.
Clinical management should be based upon the pregnant patient's Rh blood type result by routine serology. A repeat specimen is not indicated.

RESULT DETAILS: ANEUPLOIDIES

Condition Tested [1]	*Result*	*Risk Before Test* [2]	*Risk After Test* [3]
Trisomy 21	Low Risk	1/152	<1/10,000
Trisomy 18	Low Risk	1/354	<1/10,000
Trisomy 13	Low Risk	1/1,116	<1/10,000
Monosomy X	Low Risk	1/255	<1/10,000
Triploidy	Low Risk		

RESULT DETAILS: MICRODELETIONS

Condition Tested [1]	*Result*	*Risk Before Test* [2]	*Risk After Test* [4]
22q11.2 deletion syndrome	Low Risk	1/2,000	1/9,000
1p36 deletion syndrome	Low Risk	1/5,000	1/12,400
Angelman syndrome	Low Risk	1/12,000	1/16,600
Cri-du-chat syndrome	Low Risk	1/20,000	1/57,100
Prader-Willi syndrome	Low Risk	1/10,000	1/13,800

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Risk after test for aneuploidy incorporates results from the Panorama algorithm and data from a published population study of over 1 million women [DiNonno et al.J.Clin.Med.2019.Aug 26; 8(9):1311.doi:10.3390/jcm8091311] and are reported as PPVs (high risk) and NPVs (low risk). Maternal age and fetal fraction are utilized in this calculation; however, the "risk after test" may not reflect the actual PPVs for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, and personal/family history, are not included in the risk assessment. 4. Risk after test for microdeletion(s) incorporates results from the Panorama algorithm and data from multiple studies [Dar P et al. Cell-free DNA screening for prenatal detection of 22q11.2 deletion syndrome, American Journal of Obstetrics and Gynecology (2022), https://doi.org/10.1016/j.ajog.2022.01.002; Martin et al. Clin Genetics. 2017 Jul 11, Wapner R J et al. Am J Obstst Gynecol. 2015 Mar;212 (3):332 .e1-9] and are reported as PPVs (high risk) and NPVs (low risk). Risks for microdeletions are independent of maternal age and fetal fraction is utilized in this calculation; however, the "risk after test" may not reflect the actual PPV for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, personal/family history, are not included in the risk assessment.

Patient Information	
Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/ 0 days
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Test Information	
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Additional Reports:	N/A
Report Date:	02/01/2013
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Testing Methodology: DNA isolated from maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay and is sequenced using a high-throughput sequencer. Fetal fraction is determined using a proprietary algorithm incorporating data from single nucleotide polymorphism-based (SNP-based) next-generation sequencing [Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8]. If there is sufficient fetal fraction, sequencing data is analyzed using a proprietary SNP-based algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X and Y. If ordered, specific microdeletions will be evaluated using similar methodology [Wapner RJ et al. Am J Obstet Gynecol. 2015 Mar;212(3):332.e1-9]. If the fetal fraction is insufficient, an additional algorithm to determine whether there is an increased risk for triploidy, trisomy 18, and trisomy 13 may be utilized, known as fetal fraction based risk assessment (FFBR) [McKanna et al. Ultrasound Obstet Gynecol 2019; 53:73-79]. If ordered, and pregnant patient is RhD negative by genotype, fetal RhD status will be evaluated using similar methodology if fetal fraction is sufficient [Wang et al. Detection of fetal RhD status on SNP-based prenatal cell-free DNA screening. In: American Society of Human Genetics; Nov 1-5, 2023; Washington, D.C.] However, some samples will not produce a result due to failure to meet the necessary quality thresholds.

This test has been validated on women with a singleton, twin or egg donor pregnancy of at least nine weeks gestation. A result will not be available for higher order multiples and multiple gestation pregnancies with an egg donor or surrogate, or bone marrow transplant recipients. Complete test panel is not available for twin gestations and pregnancies achieved with an egg donor or surrogate. For twin pregnancies with a fetal fraction value below the threshold for analysis, a sum of the fetal fractions for both twins will be reported. As this assay is a screening test and not diagnostic, false positives and false negatives can occur.

High risk aneuploidy and microdeletion test results need diagnostic confirmation by alternative testing methods. Low risk results do not fully exclude the diagnosis of any of the syndromes nor do they exclude the possibility of other chromosomal abnormalities or birth defects, which are not a part of this test. Potential sources of inaccurate results include, but are not limited to, mosaicism, low fetal fraction, limitations of current diagnostic techniques, or phlebotomy labeling errors. This test will not identify all deletions associated with each microdeletion syndrome. This test has been validated for deletions ≥0.5 Mb within the 22q11.2 A-D region. This test has been validated on full region deletions only for 1p36 deletion syndrome, Cri-du-chat syndrome, Prader Willi syndrome and Angelman syndrome and may be unable to detect smaller deletions. Microdeletion risk score may be dependent upon fetal fraction, as deletions on the maternally inherited copy are difficult to identify at lower fetal fractions. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate.

Fetal RhD non-invasive prenatal test does not replace the pregnant patient's serology result. False positive results may occur due to the presence of rare genotypes that include but are not limited to Weak D, Partial D, or RhD Pseudogene. False negative results, while rare, can also occur. Additional potential sources of inaccurate results include, but are not limited to, phlebotomy labeling errors, low fetal fraction, sample contamination, low DNA quantity, or low number of sequencing reads. Fetal RhD status will not be assessed for dizygotic twin pregnancies or in the context of certain maternal genetic variants. Test results should always be interpreted by a clinician in the context of clinical and familial data.

Reviewed By: Wenbo Xu, M.D., Ph.D., FACMG, Senior Laboratory Director

CLIA Laboratory Director: J. Dianne Keen-Kim, Ph.D., FACMG

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 844-778-4700, option 2. Ask for the NIPT genetic counselor on call.

Patient Information

Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/ 0 days
Maternal Weight:	N/A
Patient ID:	P99457
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Test Information

Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
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OVERALL TEST SPECIFICATIONS FOR PANORAMA

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value (PPV) is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 95% chance that the fetus is affected by Trisomy 21. In other words, 5% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value (NPV) is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*PPV*	*NPV*
Trisomy 21 [1.,1.]	99.0% (CI 97.1-100)	>99% (CI 99.93-99.99)	95%	>99.99%
Trisomy 18 [1.,1.]	94.1% (CI 82.9-100)	>99% (CI 99.96-100)	91%	>99.99%
Trisomy 13 [1.,1.]	>99% (CI 73.5-100)	>99% (CI 99.6-100)	68%	>99.99%
Monosomy X [1.,1.]	94.7% (CI 74.0-99.9)	>99% (CI 99.7-100)	78%	>99.99%
Triploidy [1.,1.]	>99% (CI 66.4-100)	>99% (CI 99.5-100)	7.5%	>99.99%
XXX, XXY, XYY [1.]	73.1% (CI 61.0-85.1)	99.9% (CI 99.90-99.99)	86.4%	99.87%
22q11.2 deletion syndrome [1.]	83.3% (CI 51.6-97.9)	>99% (CI 99.91-99.98)	53%	99.9% (CI 99.9-100)
1p36 deletion syndrome [1.,1.]	>99% (CI 2.5-100)	>99% (CI 99.1-100)	7-17%	99.98-99.99%
Angelman syndrome [1.,1.]	95.5% (CI 77.2-99.9)	>99% (CI 99.1-100)	10%	>99.99%
Cri-du-chat syndrome [1.,1.]	>99% (CI 85.8-100)	>99% (CI 99.1-100)	2-5%	>99.99%
Prader-Willi syndrome [1.,1.]	93.8% (CI 69.8-99.8)	>99% (CI 99.1-100)	5%	>99.99%
Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		
Fetal RhD+ [1.]	>99.9% (CI 98.9 - 100)	99.3% (CI 97.6 - 99.8)	99.4%	>99.99%

1. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.019
1. DiNonno W et al. J Clin Med. 2019. 26;8(9):1311. doi: https://doi.org/10.3390/jcm8091311
1. Martin et al. ISUOG World Congress 2022: September, 2022
1. Nicolaides KH et al. Fetal Diagn Ther. 2014. 35;(3):212-7. doi: https://doi.org/10.1159/000355655
1. Kantor et al. Prenat Diagn. 2022. 42;(8): 994-999. Doi: 10.1002/pd.6169
1. Martin K et al. ISPD 25th International Conference: June, 2021
1. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.002
1. Martin K et al. Clin Genet. 2018. 93(2):293-300. doi: https://doi.org/10.1111/cge.13098
1. Wapner RJ et al. Am J Obstet Gynecol. 2015. 212(3):332.e1-9. doi: https://doi.org/10.1016/j.ajog.2014.11.041
1. Natera internal validation data, 2024

Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.
Sex chromosome trisomies are only reported when clearly identified. At lower fetal fractions, identification of sex chromosome trisomies may not be possible.
Dependent upon fetal fraction. For 22q11.2 deletion syndrome, only the paternal allele is evaluated at FF ≤6.5%. For 1p36 deletion syndrome and Cri-du-chat syndrome, only the paternal allele is evaluated at FF <7%. For Angelman syndrome, no risk assessment is reported at FF<7%. For Prader-Willi syndrome, no risk assessment is reported at FF≤2.8%.

Test specifications above are applicable to singleton and monozygotic twin pregnancies only. For additional information, please visit: ***www.natera.com/panorama-test/test-specs***

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Understanding Your Results

Low risk

What do my results mean?

Your results show that there is a low risk to your baby for the chromosome conditions listed on the report. These results cannot tell with certainty that your baby does not have these conditions. The specific chance that your baby has each condition can be found on page 1 of your test report under "Risk after test." Most people with low risk results do not choose to have further testing for these chromosome conditions.[1]

What should I do next?

You should talk to your healthcare provider about these results and continue with the prenatal care recommended for you. Although the chance that your baby has these chromosome conditions is low, you have the option of doing further testing during pregnancy to find out for sure if your baby has these conditions. These tests are called CVS (chorionic villus sampling) and amniocentesis, and both have a small risk of miscarriage. Please talk to your healthcare provider if you have questions about further testing.

NEVA* is always available to help you learn about your results. You can connect with Natera's Educational Virtual Assistant (NEVA) by logging into the patient portal at my.natera.com.

*NEVA is available only in the United States.

If you would like to discuss your results with a Natera genetic counselor, you can schedule a free information session at naterasession.com, by texting SESSION to 636363*, or by calling +1.877.476.4743. Please select **Panorama Non-Invasive Prenatal Chromosome Screening Post-Test** as the appointment type.

You can find a local genetic counselor through the National Society of Genetic Counselors at findageneticcounselor.nsgc.org.

*Text scheduling is available only in the United States.

1. van Schendel RV, et al; Dutch NIPT Consortium. Women's Experience with Non-Invasive Prenatal Testing and Emotional Well-being and Satisfaction after Test-Results. J Genet Couns. 2017 Dec;26(6):1348-1356. doi: 10.1007/s10897-017-0118-3. Epub 2017 Jun 30. PMID: 28667567; PMCID: PMC5672853.

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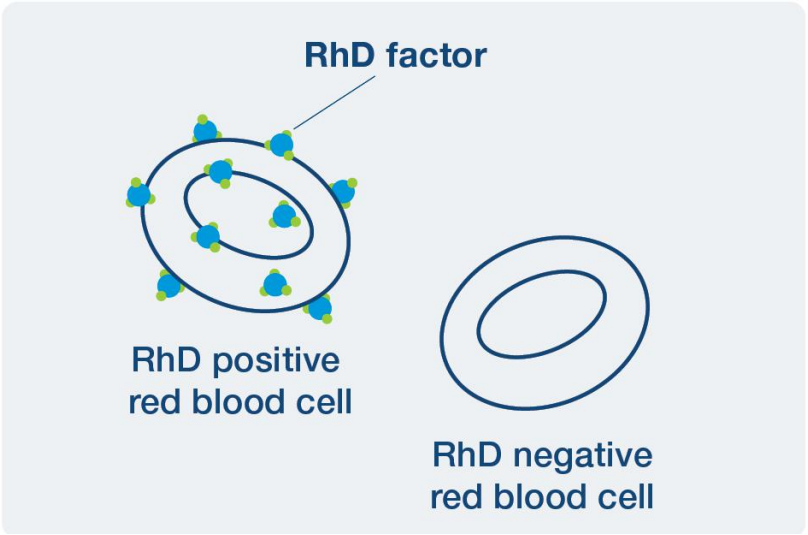
Understanding Your Results

Baby's predicted RhD factor not determined

What does this result mean?

This result means that your baby's RhD factor was not determined. There are two main reasons that a baby's RhD factor is not determined by this test. First, your own RhD factor could mean that it is not necessary to determine your baby's RhD factor. Second, sometimes the lab is not able to perform the test due to technical limitations.

What is RhD testing and why is it important in pregnancy?



RhD factor is a protein that can be present or absent on the surface of a person's red blood cells. RhD positive means that someone's red blood cells have the RhD protein on them. People who are RhD negative have red blood cells without this protein. The RhD factor can cause problems in a pregnancy if an RhD negative pregnant person's blood is mixed with RhD positive blood from the baby. When this happens, the RhD negative person's body will recognize the RhD factor on the RhD positive blood cells from the baby as foreign and will make antibodies to fight the RhD factor. When a pregnant person has RhD factor antibodies, they are said to be sensitized. If a sensitized pregnant person is carrying an RhD positive baby, the antibodies can cross the placenta and attack the baby's red blood cells. The antibodies can cause a loss of red blood cells, which can lead to serious health problems for the baby. When a pregnant person and their baby have different RhD factors, it is called RhD incompatibility.

Can I repeat this test to get an answer?

It depends on the reason that you did not get a result. Your lab report could say one of two things.

1. **Fetal status not assessed.** If your lab report says this, you should not repeat this test. You can get this result for one of two reasons.

    - "Fetal status not assessed" could mean that you are RhD positive. RhD incompatibility is not a risk to your baby if you are RhD positive.

    - Rarely, a result of "fetal status not assessed" could mean that you are RhD negative due to having what is called the *RHD* pseudogene. When a pregnant person has the *RHD* pseudogene, the lab does not determine the baby's RhD factor.

If your lab report says, "fetal status not assessed," please talk to your healthcare provider about looking at the results of other blood tests you had during pregnancy to determine what to do next.

2. **No results for fetal *RHD*.** If your lab report says this, the lab was not able to get a result. There are a few different reasons the lab would not be able to get a result. The reason you did not get a result is listed on your report. Sometimes this problem will not be solved by sending another blood sample. Many times the lab will be able to get a result on another sample. If another sample can be sent, your lab report will say so.

What should I do next?

Talk to your healthcare provider about next steps. Looking at the results of other blood tests you have had during pregnancy can sometimes help to explain this result. Sometimes your healthcare provider will recommend different blood tests, or it can sometimes be helpful to repeat this test. If you are RhD negative and it is important to know the baby's RhD factor, you could have the option of a test called CVS (chorionic villus sampling) or amniocentesis. These tests can tell you your baby's RhD factor. Both tests have a small risk of miscarriage.

Please talk to your healthcare provider about your result. If you would also like to discuss your result with a Natera genetic counselor, you can schedule a free information session at natera session.com, by texting* **SESSION** to **636363**, or by calling **1.877.467.4743**. Please select **Panorama non-invasive prenatal chromosome screening, post-test** as the appointment type.

You can find a local genetic counselor through the National Society of Genetic Counselors at findageneticcounselor.nsgc.org.

*Text scheduling is available only in the United States

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Patient Information	
Patient Name:	Jane Doe
Date of Birth:	11/08/1975
Maternal Age at EDD:	37
Gestational Age:	11 weeks/ 0 days
Maternal Weight:	N/A
Patient ID:	P99457
Medical Record #:	M84555
Collection Kit:	123233-2-N
Reference ID:	254233-2-N
Accessioning ID:	C47695
Case File ID:	-159466

Test Information	
Ordering Physician:	Dr. Matthew Goodbirth, M.D. (G123456)
Clinic Information:	Natera, Inc.
Additional Reports:	N/A
Report Date:	02/01/2013
Samples Collected:	01/31/2013
Samples Received:	02/01/2013
	Mother Blood

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FINAL RESULTS SUMMARY:

ANEUPLOIDIES AND MICRODELETIONS

Result
LOW RISK

Fetal Sex
Male

Fetal Fraction(s)
8.3%

Notes by the clinical reviewer, if any, will be shown here.

FETAL RHD

Result
RHD positive

This is a screening test only.

RESULT DETAILS: ANEUPLOIDIES

Condition Tested [1]	*Result*	*Risk Before Test* [2]	*Risk After Test* [3]
Trisomy 21	Low Risk	1/152	<1/10,000
Trisomy 18	Low Risk	1/354	<1/10,000
Trisomy 13	Low Risk	1/1,116	<1/10,000
Monosomy X	Low Risk	1/255	<1/10,000
Triploidy	Low Risk		

RESULT DETAILS: MICRODELETIONS

Condition Tested [1]	*Result*	*Risk Before Test* [2]	*Risk After Test* [4]
22q11.2 deletion syndrome	Low Risk	1/2,000	1/9,000

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Risk after test for aneuploidy incorporates results from the Panorama algorithm and data from a published population study of over 1 million women [DiNonno et al.J.Clin.Med.2019.Aug 26; 8(9):1311.doi:10.3390/jcm8091311] and are reported as PPVs (high risk) and NPVs (low risk). Maternal age and fetal fraction are utilized in this calculation; however, the "risk after test" may not reflect the actual PPVs for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, and personal/family history, are not included in the risk assessment. 4. Risk after test for microdeletion(s) incorporates results from the Panorama algorithm and data from multiple studies [Dar P et al. Cell-free DNA screening for prenatal detection of 22q11.2 deletion syndrome, American Journal of Obstetrics and Gynecology (2022), https://doi.org/10.1016/j.ajog.2022.01.002; Martin et al. Clin Genetics. 2017 Jul 11, Wapner R J et al. Am J Obstst Gynecol. 2015 Mar;212 (3):332 .e1-9] and are reported as PPVs (high risk) and NPVs (low risk). Risks for microdeletions are independent of maternal age and fetal fraction is utilized in this calculation; however, the "risk after test" may not reflect the actual PPV for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, personal/family history, are not included in the risk assessment.

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Testing Methodology: DNA isolated from maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay and is sequenced using a high-throughput sequencer. Fetal fraction is determined using a proprietary algorithm incorporating data from single nucleotide polymorphism-based (SNP-based) next-generation sequencing [Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8]. If there is sufficient fetal fraction, sequencing data is analyzed using a proprietary SNP-based algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X and Y. If ordered, specific microdeletions will be evaluated using similar methodology [Wapner RJ et al. Am J Obstet Gynecol. 2015 Mar;212(3):332.e1-9]. If the fetal fraction is insufficient, an additional algorithm to determine whether there is an increased risk for triploidy, trisomy 18, and trisomy 13 may be utilized, known as fetal fraction based risk assessment (FFBR) [McKanna et al. Ultrasound Obstet Gynecol 2019; 53:73-79]. If ordered, and pregnant patient is RhD negative by genotype, fetal RhD status will be evaluated using similar methodology if fetal fraction is sufficient [Wang et al. Detection of fetal RhD status on SNP-based prenatal cell-free DNA screening. In: American Society of Human Genetics; Nov 1-5, 2023; Washington, D.C.] However, some samples will not produce a result due to failure to meet the necessary quality thresholds.

This test has been validated on women with a singleton, twin or egg donor pregnancy of at least nine weeks gestation. A result will not be available for higher order multiples and multiple gestation pregnancies with an egg donor or surrogate, or bone marrow transplant recipients. Complete test panel is not available for twin gestations and pregnancies achieved with an egg donor or surrogate. For twin pregnancies with a fetal fraction value below the threshold for analysis, a sum of the fetal fractions for both twins will be reported. As this assay is a screening test and not diagnostic, false positives and false negatives can occur.

High risk aneuploidy and microdeletion test results need diagnostic confirmation by alternative testing methods. Low risk results do not fully exclude the diagnosis of any of the syndromes nor do they exclude the possibility of other chromosomal abnormalities or birth defects, which are not a part of this test. Potential sources of inaccurate results include, but are not limited to, mosaicism, low fetal fraction, limitations of current diagnostic techniques, or phlebotomy labeling errors. This test will not identify all deletions associated with each microdeletion syndrome. This test has been validated for deletions ≥0.5 Mb within the 22q11.2 A-D region. This test has been validated on full region deletions only for 1p36 deletion syndrome, Cri-du-chat syndrome, Prader Willi syndrome and Angelman syndrome and may be unable to detect smaller deletions. Microdeletion risk score may be dependent upon fetal fraction, as deletions on the maternally inherited copy are difficult to identify at lower fetal fractions. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate.

Fetal RhD non-invasive prenatal test does not replace the pregnant patient's serology result. False positive results may occur due to the presence of rare genotypes that include but are not limited to Weak D, Partial D, or RhD Pseudogene. False negative results, while rare, can also occur. Additional potential sources of inaccurate results include, but are not limited to, phlebotomy labeling errors, low fetal fraction, sample contamination, low DNA quantity, or low number of sequencing reads. Fetal RhD status will not be assessed for dizygotic twin pregnancies or in the context of certain maternal genetic variants. Test results should always be interpreted by a clinician in the context of clinical and familial data.

Reviewed By: Wenbo Xu, M.D., Ph.D., FACMG, Senior Laboratory Director

CLIA Laboratory Director: J. Dianne Keen-Kim, Ph.D., FACMG

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 844-778-4700, option 2. Ask for the NIPT genetic counselor on call.

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OVERALL TEST SPECIFICATIONS FOR PANORAMA

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value (PPV) is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 95% chance that the fetus is affected by Trisomy 21. In other words, 5% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value (NPV) is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*PPV*	*NPV*
Trisomy 21 [1.,1.]	99.0% (CI 97.1-100)	>99% (CI 99.93-99.99)	95%	>99.99%
Trisomy 18 [1.,1.]	94.1% (CI 82.9-100)	>99% (CI 99.96-100)	91%	>99.99%
Trisomy 13 [1.,1.]	>99% (CI 73.5-100)	>99% (CI 99.6-100)	68%	>99.99%
Monosomy X [1.,1.]	94.7% (CI 74.0-99.9)	>99% (CI 99.7-100)	78%	>99.99%
Triploidy [1.,1.]	>99% (CI 66.4-100)	>99% (CI 99.5-100)	7.5%	>99.99%
XXX, XXY, XYY [1.]	73.1% (CI 61.0-85.1)	99.9% (CI 99.90-99.99)	86.4%	99.87%
22q11.2 deletion syndrome [1.]	83.3% (CI 51.6-97.9)	>99% (CI 99.91-99.98)	53%	99.9% (CI 99.9-100)
Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		
Fetal RhD+ [1.]	>99.9% (CI 98.9 - 100)	99.3% (CI 97.6 - 99.8)	99.4%	>99.99%

1. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.019
1. DiNonno W et al. J Clin Med. 2019. 26;8(9):1311. doi: https://doi.org/10.3390/jcm8091311
1. Martin et al. ISUOG World Congress 2022: September, 2022
1. Nicolaides KH et al. Fetal Diagn Ther. 2014. 35;(3):212-7. doi: https://doi.org/10.1159/000355655
1. Kantor et al. Prenat Diagn. 2022. 42;(8): 994-999. Doi: 10.1002/pd.6169
1. Martin K et al. ISPD 25th International Conference: June, 2021
1. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.002
1. Natera internal validation data, 2024

Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.
Sex chromosome trisomies are only reported when clearly identified. At lower fetal fractions, identification of sex chromosome trisomies may not be possible.
Dependent upon fetal fraction. For 22q11.2 deletion syndrome, only the paternal allele is evaluated at FF ≤6.5%. For 1p36 deletion syndrome and Cri-du-chat syndrome, only the paternal allele is evaluated at FF <7%. For Angelman syndrome, no risk assessment is reported at FF<7%. For Prader-Willi syndrome, no risk assessment is reported at FF≤2.8%.

Test specifications above are applicable to singleton and monozygotic twin pregnancies only. For additional information, please visit: ***www.natera.com/panorama-test/test-specs***

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Understanding Your Results

Low risk

What do my results mean?

Your results show that there is a low risk to your baby for the chromosome conditions listed on the report. These results cannot tell with certainty that your baby does not have these conditions. The specific chance that your baby has each condition can be found on page 1 of your test report under "Risk after test." Most people with low risk results do not choose to have further testing for these chromosome conditions.[1]

What should I do next?

You should talk to your healthcare provider about these results and continue with the prenatal care recommended for you. Although the chance that your baby has these chromosome conditions is low, you have the option of doing further testing during pregnancy to find out for sure if your baby has these conditions. These tests are called CVS (chorionic villus sampling) and amniocentesis, and both have a small risk of miscarriage. Please talk to your healthcare provider if you have questions about further testing.

NEVA* is always available to help you learn about your results. You can connect with Natera's Educational Virtual Assistant (NEVA) by logging into the patient portal at my.natera.com.

*NEVA is available only in the United States.

If you would like to discuss your results with a Natera genetic counselor, you can schedule a free information session at naterasession.com, by texting SESSION to 636363*, or by calling +1.877.476.4743. Please select **Panorama Non-Invasive Prenatal Chromosome Screening Post-Test** as the appointment type.

You can find a local genetic counselor through the National Society of Genetic Counselors at findageneticcounselor.nsgc.org.

*Text scheduling is available only in the United States.

1. van Schendel RV, et al; Dutch NIPT Consortium. Women's Experience with Non-Invasive Prenatal Testing and Emotional Well-being and Satisfaction after Test-Results. J Genet Couns. 2017 Dec;26(6):1348-1356. doi: 10.1007/s10897-017-0118-3. Epub 2017 Jun 30. PMID: 28667567; PMCID: PMC5672853.

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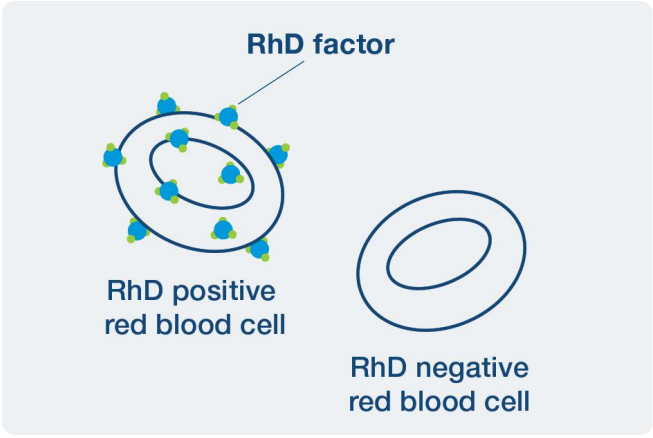
Understanding Your Results

Baby's predicted RhD factor – positive

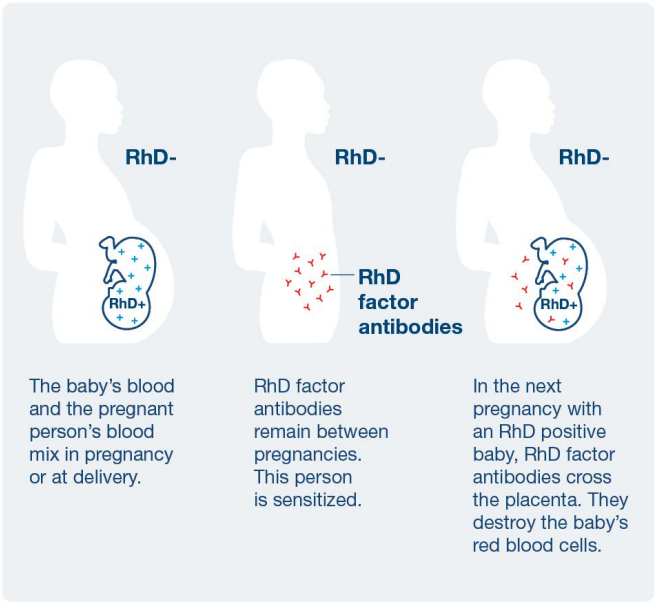
What does this result mean?

This result means that your baby is likely RhD positive. RhD positive means that red blood cells have a protein on them called the RhD factor (also known as RhD antigen). People who are RhD negative have red blood cells without this protein. Your result also shows that you are likely RhD negative.



Why is the RhD factor important in pregnancy?

The RhD factor can cause problems in a pregnancy if an RhD negative person is *sensitized* and is carrying an RhD positive baby. A person is sensitized when they have RhD antibodies. Antibodies are made by the immune system. They attach to things that are foreign to the body, like viruses, and destroy them. An RhD negative person carrying an RhD positive baby can become sensitized if their blood mixes with the baby's blood. Their body will see the baby's red blood cells with the RhD factor as foreign and will create antibodies to attack any cells with the RhD factor. Having RhD antibodies is not usually a problem during the pregnancy when the antibodies are first made. But, if the RhD negative person has another pregnancy with an RhD positive baby, they will still have the RhD factor antibodies. The antibodies can cross the placenta and attack the baby's red blood cells. This baby's red blood cells will be destroyed, causing anemia, or hemolytic disease. Anemia is having too few red blood cells. Red blood cells are important because they carry oxygen to the body's tissues. There is a medication that can help to prevent sensitization.



How would my blood and the baby's blood mix?

Generally, it is true that a pregnant person's blood and a baby's blood do not mix. A small number of red blood cells can cross the placenta. Rarely, this small number of cells can be enough to cause sensitization.

Certain events can make it more likely that a baby's blood and a pregnant person's blood will mix. These events can include vaginal bleeding, CVS, and amniocentesis. A person can also become sensitized due to an ectopic pregnancy, miscarriage, or delivery of an RhD positive baby. Antibodies made during or after a pregnancy remain in the body forever. They are present for all future pregnancies. Once someone is sensitized, they will always be sensitized.

What should I do next?

Talk to your healthcare provider. They will come up with a plan for prevention or treatment. A blood test called an antibody screen can find out if you are sensitized.

- If you are RhD negative and unsensitized, you will likely be offered a medication called RhD immune globulin.* This medication can typically prevent you from becoming sensitized. It is recommended that you have it around 28 weeks gestation and again within 72 hours of delivery if your baby is RhD positive.** Your baby's Rh factor will be tested after delivery, usually with blood from the umbilical cord. This testing is done to confirm that the result of this screening test is correct and your baby is RhD positive.

- If you are RhD negative and sensitized (have RhD antibodies), your healthcare provider will make a plan for how to monitor your baby for anemia during pregnancy. There are treatments for anemia that can happen during or after pregnancy, if needed.

*RhoGAM, Rhophylac, WinRho, or equivalent medications.
**The American College of Obstetricians and Gynecologists in the United States (2017) and the medical organizations of many other countries (2021) have similar recommendations.[1,2,3,4] Please talk to your healthcare provider about current recommendations where you live. Your care could also depend on your history and other factors specific to you.

Please talk to your healthcare provider about your result. If you would also like to discuss your result with a Natera genetic counselor, you can schedule a free information session at **natera session.com**, by texting* **SESSION** to **636363**, or by calling **1.877.467.4743**. Please select **Panorama non-invasive prenatal chromosome screening, post-test** as the appointment type.

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References:
1. Practice Bulletin No. 181: Prevention of Rh D Alloimmunization. Obstetrics & Gynecology. 2017; 130 (2): e57-e70. doi: 10.1097/AOG.0000000000002232.
2. Toly-Ndour C et al. (2021). Rh disease prevention: the European Perspective. ISBT Science Series, 16(1), 106–118. https://doi.org/10.1111/voxs.12617
3. Prevention Rhesus disease. (2021) In nhs.uk. Retreived 13 Feb 2024 from https://www.nhs.uk/conditions/rhesus-disease/prevention/.
4. Visser GHA et al; FIGO Committee for Safe Motherhood, Newborn Health. FIGO/ICM guidelines for preventing Rhesus disease: A call to action. Int J Gynaecol Obstet. 2021 Feb;152(2):144-147. doi: 10.1002/ijgo.13459. Epub 2021 Jan 9. PMID: 33128246; PMCID: PMC7898700.

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