

Panorama: the next generation of NIPT

Screens for:

Singleton pregancies

- Trisomies 21, 18, 13
- Monosomy X
- Triploidy
- Sex chromosome trisomies*
 20 at 1.0 deletion syndrome
- 22q11.2 deletion syndrome (optional)
- Additional microdeletion syndromes (optional)
- Fetal sex (optional)

Twin pregancies

- Zygosity
- Trisomies 21, 18, 13
- Fetal sex for each twin (optional)

If screening reveals monozygotic twins, Panorama can additionally screen for:

- Monosomy X
- Sex chromosome trisomies*
- 22q11.2 deletion syndrome (optional)

Egg donor or surrogate pregnancies

(Singleton pregnancies only)

- Trisomies 21, 18, 13
- Fetal sex (optional)

*Reported when suspected

Non-invasive prenatal screen



Panorama's unique SNP-based technology enables more comprehensive screening with greater accuracy in validation¹⁻¹⁶



Only Panorama distinguishes between maternal and fetal (placental) DNA



Panorama reduces both false negative rates (FNR) and false positive rates (FPR) compared to other NIPTs

Combined FNR in validation studies (T21, T18, T13) Combined FPR in validation studies (T21, T18, T13, MX)



Panorama's SNP-based technology results in the highest fetal sex accuracy of any NIPT in validation studies

Other NIPTs may report incorrect gender for as many as 1 in 77 cases. A wrong call can lead to unnecessary clinical work-up and create anxiety for the patient.



Panorama's SNP-based approach yields the highest commercially available sensitivity for the most common ~3Mb 22q11.2 deletion

For small deletions like 22q11.2, Panorama's ability to evaluate unique DNA sequences within the region of interest enables better detection.



*Based on a validation study of 419 samples, in which Panorama correctly identified 9/10 samples that were positive for 22q11.2. Only the paternal allele is evaluated at fetal fractions < 6.5%.

Accurate fetal fraction measurement is essential for accurate results²²

Panorama is the only NIPT that has always measured and reported fetal fraction

Panorama's SNP-based method is a gold standard in fetal fraction measurement
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	Panorama ^{1,2,3}	Harmony ^{4,23}	MaterniT21 ^{5,6,7,24}	Verifi ^{10,11,12}	Illumina platforms
Method of fetal fraction measurement	13,392 SNPs	576 SNPs	Distribution of short (<150 bp) cfDNA	No data available on methodology or performance	No data available on methodology or performance
Combined false negative rate in validation studies (trisomies 21, 18, 13)	0.60%	1.33%	1.89%	2.40%	No published data

Counting methodologies' ability to detect abnormalities decreases below 8% fetal fraction, which may increase false negative results^{25,26}



Deeper sequencing on chromosomal regions of interest enables Panorama to maintain highquality results at lower fetal fractions

fetal fraction to a higher depth of read. Verifi 25 Verifi²⁷ 400 7X-29X-Panorama **Panorama** when fetal (reflex 2600 720 fraction positive is <5%²⁸ results) 0 1000 2000 3000 0 250 500 750 1000 Chromosome 21 (thousands) 22q (thousands)

Panorama's proprietary algorithm incorporates fetal fraction measurement and reflexes samples with lower

Panorama for twin pregnancies

Only Panorama reports zygosity, individual fetal fractions for dizygotic twins, and fetal sex for each twin¹⁶

	Panorama ¹⁶	Harmony ^{29,30}	MaterniT21 ³¹	Verifi ³²	Illumina platforms ^{33,34,35,36}
Zygosity	<	×	×	×	×
Individual fetal fractions	<	×	×	×	×
Fetal sex for each twin	<	×	×	×	×
Trisomies 21, 18, 13	<	\checkmark	\checkmark	V	\checkmark
Monosomy X*	<	×	×	×	×
22q11.2 deletion syndrome*	<₽*	×	\checkmark	×	×

*Available for monozygotic twins only

Zygosity	Fetal Sex	Fetal Fraction(s)
Dizygotic	🔿 Male	
FRATERNAL TWINS	Q Female	8.3%, 8.4%
	Zygosity Dizygotic FRATERNAL TWINS	ZygosityFetal SexDizygoticO MaleFRATERNAL TWINSPemale

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

Panorama allows clinicians to align their ultrasound findings with early and accurate zygosity information

Chorionicity is the strongest predictor for pregnancy complications in twins.³⁷ Studies have shown that up to 19% of monochorionic pregnancies are incorrectly classified as dichorionic using ultrasound.³⁸



- Higher risk for twin-twin transfusion syndrome (TTTS), birth defects, etc. if monochorionic
- Consider early MFM referral to confirm chorionicity
- Develop tailored care plan for pregnancy



- All dizygotic pregnancies are dichorionic
- Low risk for TTTS
- Continue standard care for pregnancy

Fetal fraction measurement and reporting in twins is important for reliable NIPT results



Fetal fraction is, on average, 30% higher in twin pregnancies, but fetal fraction per twin is lower compared to singleton pregnancies.²⁸

Provider support



Proactive billing outreach and price transparency



Complimentary mobile phlebotomy services and in-office phlebotomist for our testing*



Direct support from board-certified genetic counselors; call 650.249.9090 or email niptgc@natera.com for:

- Clinical questions
- Consultations on high-risk results
- Regional medical education and support



Our Natera Connect provider portal can be accessed online at connect.natera.com to:

- Order and track tests electronically
- Release low-risk results to patients (optional)

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References

- Nicolaides et al. Prenat Diagn. 2013 June; 33(6):575-9. 1.
- Pergament et al. Obstet Gynecol. 2014 Aug; 124(2 Pt 1):210-8.
- 3. Ryan et al. Fetal Diagn Ther. 2016;40(3):219-223. 4.
- Stokowski et al. Prenat Diagn. 2015 Dec; 35(12):1243-6. Jones et al. Ultrasound Obstet Gynecol. Accepted manuscript. DOI: 10.1002/uog.18986 5.
- Palomaki et al. Genet Med. 2011 Nov; 13(11):913-20. 6
- Palomaki et al. Genet Med. 2012 Mar; 14(3):296-305. 8.
- Porreco et al. Am J Obstet Gynecol 2014;211:365.e1-12.
- 9. Mazloom et al. Prenat Diagn 2013 Jun; 33(6):591-7.
- 10. Sehnert et al. Clinical Chemistry 2011 Jun;57(7):1042-1049. 11. Bianchi et al. Obstet Gynecol. 2012 May: 119(5):890-901.
- 12. Bianchi et al. N Engl J Med 2014;370:799-808.
- 13. Nicolaides et al. Fetal Diagn Ther. 2014:35(3):212-7.
- 14. Curnow et al. Am J Obstet Gynecol. 2015 Jan; 212(1):79.e1-9.
- 15. Samango-Sprouse et al. Prenat Diagn. 2013;33:1-7.
- 16. Natera validation data for twin pregnancies. Manuscript in preparation.
- 17. Verinata white paper. Analytical validation of the Veri prenatal test. 2012.
- 18. Norvez et al. The European Human Genetics Conference, ESHG. Copenhagen,
- Denmark. May 27-30, 2017. 19. Schmid et al. Fetal Diagn Ther. 2017, DOI: 10.1159/000484317.

Patient support



Patients can learn about testing, book services, and track test results through our patient portal at my.natera.com



Complimentary mobile phlebotomy services can be scheduled by calling 855.271.1502 and pressing option 1



Complimentary pre- and post-test genetic information sessions with a board certified genetic counselor can be scheduled by calling 855.271.1502 and pressing option 2

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Flexible payment plans, including assistance for financial hardship, are available

*Where permitted by state law

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- 20. Tynan et al. Society for Maternal-Fetal Medicine, SMFM. Las Vegas, Nevada. Jan 23-28, 2017.
- 21. Commercial protocol not validated; Illumina marketing materials cite "Srinivasan et al. Am J Hum Genet. 2013 Feb 7; 92(2): 167–176" which does not match number of reads used in commercial testing.
- 22. American College of Obstetricians and Gynecologists (ACOG/SMFM), #640, Sept 2015.
- 23. Juneau et al. Fetal Diagn Ther. 2014;36(4):282-6.
- 24. Kim et al. Prenatal Diagnosis 2015, 35, 810-815.
- 25. Canick, et al. Prenatal Diagnosis 2013, 33, 1-8.
- 26. Wright et al. Ultrasound Obstet Gynecol 2015: 45: 48-54.
- 27. Verifi marketing materials, 2016.
- 28. Internal data, Natera. 2017.
- 29. Gil et al. Fetal Diagn Ther 2014; 35: 204-211.
- 30. Bevilacqua et al. Ultrasound Obstet Gynecol 2015; 45: 61-66.
- 31. Canick et al. Prenat Diagn. 2012 Aug; 32(8): 730-4.
- 32. Fosler et al. Ultrasound Obstet Gynecol 2015; 45: 61-66.
- 33. Counsyl marketing materials, 2018. 34. Progenity marketing materials, 2018.
- 35. NxGen marketing materials, 2018.
- 36. BioReference marketing materials, 2018.
- 37. Society for Maternal-Fetal Medicine, Clinical guideline: Twin-twin transfusion syndrome, Jan 2013.
- 38. Blumenfeld et al. J Ultrasound in Med. 2014 Dec; 33(12):2187-92.

The tests described have been developed and their performance characteristics determined by the CLIA-certified laboratory performing the tests. These tests have not been cleared or approved by the U.S. Food and Drug Administration (FDA). Although FDA does not currently clear or approve laboratory-developed tests in the U.S., certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. © 2018 Natera, Inc. All Rights Reserved. PAN_MD_BR_2018_02_12_NAT-801513

