panorama™
prenatal screen

Accurate, comprehensive results you can trust

Panorama™ Prenatal Screen covers:

Aneuploidies

- Trisomies 21, 18 and 13
- Monosomy X
- Sex chromosome trisomies
- Triploidy / Vanishing Twin
- Fetal sex (optional)

Microdeletion Syndromes

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

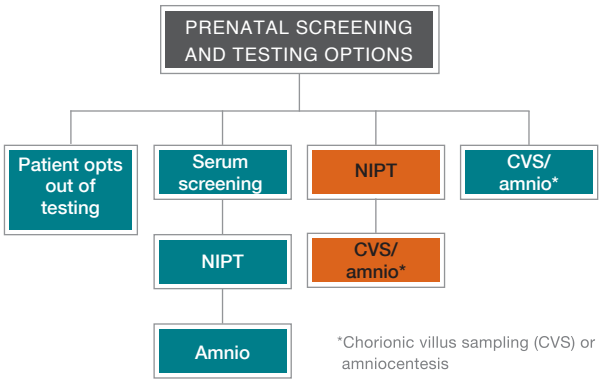
natera™
Conceive. Deliver.

Welcome to the next generation of non-invasive prenatal screening.

Only Panorama™ can distinguish between fetal and maternal DNA in the mother's blood to give you and your patient vital information about the fetus. With a comprehensive panel of chromosomal aneuploidies and microdeletions, Panorama delivers the most accurate results of any screening test, as early as 9 weeks of gestation, to help you manage your patient's pregnancy.

Non-invasive prenatal testing (NIPT) as a first line screening test

Studies indicate that NIPT is appropriate as a first line screening test for aneuploidy in all patients.[1,2,3,4,5]



*Chorionic villus sampling (CVS) or amniocentesis

- Serum screening tests for trisomies 21, 18 and 13, with sensitivity of 50 - 95% and false positive rates of approximately 5%.[6]
- Panorama, in addition to the common aneuploidies, screens for sex chromosome abnormalities, microdeletions and triploidy, identifies vanishing twin and determines fetal sex.
- Panorama's combined accuracy is >99% for aneuploidies, with a false positive rate of 0.35% for trisomies 21, 18 and 13, and Monosomy X.[1,7,8]

Both NIPT and serum screening are screening tests. Any patient with positive results indicating a potential abnormality should be offered confirmatory invasive testing via CVS or amniocentesis, or testing of the baby after delivery.[6]

Who should be screened by Panorama?

	VALIDATION T21,T18,T13 AND MX[2]		CLINICAL OUTCOMES T21, T18[1]
	Sensitivity	Specificity	PPV* (Aneuploidy Incidence)
High Risk	98.0% (98/100)	99.5% (389/391)	85.7% (2.4%)
Low Risk	100% (5/5)	100% (469/469)	88.6% (1.0%)

PPV = positive predictive value

Similar sensitivity and specificity in high and low risk cohorts validate Panorama's performance in **all pregnancies, regardless of risk,** for trisomies 21, 18, and 13, and Monosomy X.

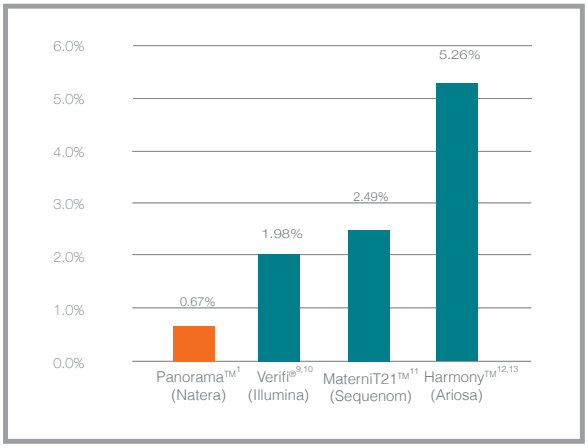
For a patient who screens as high risk on Panorama, positive predictive value (PPV) indicates the likelihood of the fetus actually being affected, and helps you and your patient decide on next steps.

Similar PPVs between high and low risk cohorts indicate that more than **8 out of 10 patients who receive a High Risk score with Panorama, regardless of pregnancy risk, will have an affected fetus.**

The Most Accurate Results

Panorama has the **lowest reported false negative rate (FNR), 0.7%**, for common aneuploidies, of any NIPT method.[1]

Combined FNR in Commercial Experience*



* Includes trisomies 21, 18 and 13, and Monosomy X.

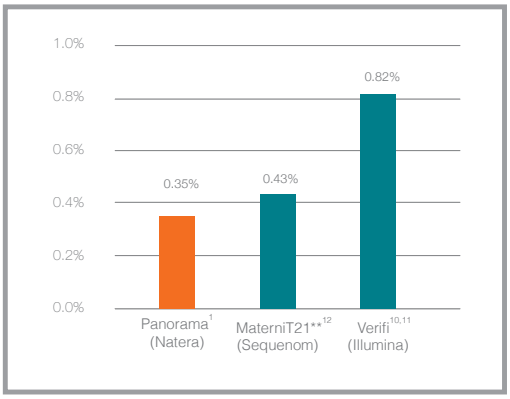
REDUCING FALSE NEGATIVES

Low fetal fraction: Up to 1/3 of all NIPT cases have a fetal fraction less than 8%, which is associated with decreased sensitivity. Panorama measures fetal fraction and adjusts its algorithm accordingly to improve sensitivity even at low fetal fractions.

Triploidy: Triploidy can be associated with serious maternal complications, such as gestational trophoblastic disease (GTD). Panorama is the only NIPT that is validated to screen for triploidy. Other NIPTs miss triploidy because they rely on the comparison of the amount of a target chromosome to that of a reference chromosome.

Panorama also has among the **lowest reported false positive rates, 0.35%,** combined for T21, T18, T13 and Monosomy X, in commercial experience.*,[1]

Combined FPR in Commercial Experience*



* Includes trisomies 21, 18 and 13, and Monosomy X. Harmony (Ariosa) is excluded from chart because data on Monosomy X is not reported in the reviewed literature.

REDUCING FALSE POSITIVES

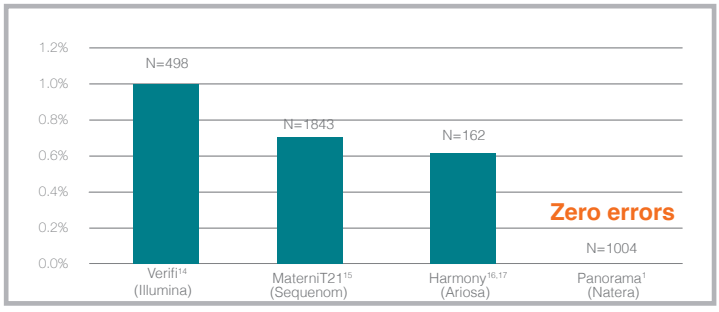
Vanishing twin: only Panorama can detect vanishing twin, which contributes to >15% of false positive results with shotgun sequencing.[9]

Maternal mosaicism: only Panorama recognizes maternal mosaicism, which is associated with up to 8.6% of false positive results when screening sex chromosomes with Verifi.[27]

** In Porreco et al. AJOG 2014, 1.4% of samples were removed due to "complex karyotype" which included all mosaic karyotypes, triploidies, and any unbalanced rearrangements with missing or duplicated genetic material. Removing these samples potentially results in the underreporting of false positives.

Panorama has **100% accuracy in fetal sex determination** in validation studies. With other NIPT methods, as many as 1 in 100 cases may report incorrect gender, leading to unnecessary anxiety and invasive procedures.

Error Rates in Fetal Sex Determination: Summary of Validation Studies



Note: Fetal sex determined by presence of Y, where Monosomy X is female.

Unparalleled accuracy for trisomy 21 and fetal sex in validation studies.

Sensitivity / False Positive Rate	Sequenom MaterniT21™ [18,19,15]	Illumina Verifi® [20,14]	Ariosa Harmony™ [21,22,16,23]	Natera Panorama™ * [2,7,8]
Trisomy 21 (Down Syndrome)	99.1% 0.1%	>99.9% 0.2%	>99% <0.1%	>99% (83/83) 0%
Trisomy 18 (Edwards Syndrome)	>99.9% 0.4%	97.4% 0.4%	>98% <0.1%	96.4% (27/28) <0.1%
Trisomy 13 (Patau Syndrome)	91.7% 0.3%	87.5% 0.1%	80% <0.1%	>99% (13/13) 0%
Monosomy X (Turner Syndrome)	94.4% 0.6%	95.0% 1.0%	91.5% 0%	92.9% (13/14) <0.1%
Sex Chromosome Trisomies	92.2%	67–100%	99%	>99% (5/5)
Female	99.1% 0.5%	97.6% 0.8%	99% 0%	>99.9% (469/469) 0%
Male	99.4% 0.9%	99.1% 1.1%	100% 1%	>99.9% (533/533) 0%
Triploidy	Unable to detect	Unable to detect	Unnable to detect	>99% (8/8)

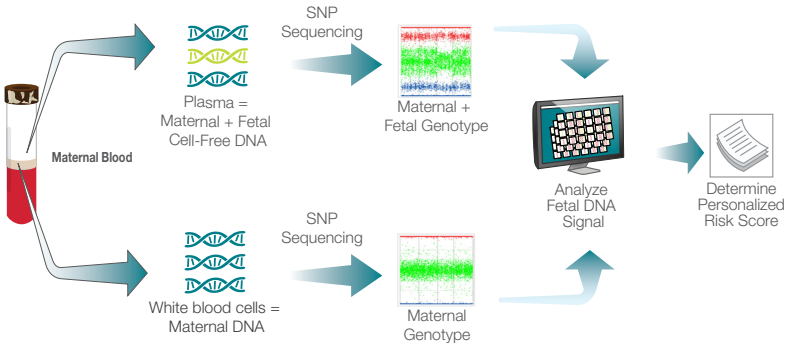
** 4 known mosaic cases were included: two Monosomy X, one T13, and one T18. Both cases of Monosomy X were called high risk, the T18 was called low risk and the T13 was no-called. False positive and false negatives can occur on all chromosomes due to maternal, fetal, and/or placental mosaicism, or other causes.*

Highest accuracy for microdeletions in validation studies.

Microdeletion Syndromes				(Partial and no results counted as negative)
Sensitivity	Sequenom MaterniT21[24]	Illumina Verifi[25]	Ariosa Harmony	Natera Panorama[26]
22q11.2 Deletion/ DiGeorge	60–86%	87.5%(7/8)	Not Offered	95.7%(45/47)
Angelman	60–86%	0%(0/1)	Not Offered	95.5%(21/22)
Cri–du–chat	85–90%	100%(2/2)	Not Offered	>99%(24/24)
1p36 Deletion	60–86%	N/A (0/0)	Not Offered	>99%(1/1)
Prader–Willi	60–86%	0%(0/1)	Not Offered	93.8%(15/16)

The Only NIPT Technology That Differentiates

Panorama is the only non-invasive prenatal screening test that distinguishes between fetal and maternal cell-free DNA thanks to SNP-based sequencing and Natera's proprietary NATUS™ (Next-Generation Aneuploidy Test Using SNPs) algorithm.



Informative reports for easier patient counseling

Panorama reports fetal fraction, individual risk score and/or PPV with each result.

REPORT SUMMARY

HIGH RISK

Notes added by the clinical reviewer, if any, will appear in place of this text.

Sex of fetus: Not reported

Fetal fraction: 14.9%

Condition tested[1]	Prior risk[2]	Panorama risk score[3]	Result	Interpretation
Trisomy 21	1/100	<1/10,000	Low Risk	
Trisomy 18	1/167	<1/10,000	Low Risk	
Trisomy 13	1/526	<1/10,000	Low Risk	
Monosomy X	1/256	<1/10,000	Low Risk	
Triploidy/Vanishing twin			Low Risk	
22q11.2 Deletion syndrome/ DiGeorge syndrome	1/2,000[4]	1/19	High Risk	Follow-up counseling and testing recommended.
1p36 Deletion syndrome	1/5,000[4]	1/12,494	Low Risk	
Angelman syndrome	1/12,000[4]	1/16,658	Low Risk	
Cri-du-chat syndrome	1/20,000[4]	1/57,110	Low Risk	
Prader-Willi syndrome	1/12,000[4]	1/13,882	Low Risk	

1. Excludes cases with evidence of fetal and/or placental mosaicism 2. Based on maternal age and gestational age 3. Based on a priori risk and test results
4. These incidences are based on overall disease prevalence in the population. This test will not identify all deletions associated with each disorder. Ability to detect deletions will be based on size and location.

TESTING METHODOLOGY: DNA isolated from the maternal blood, which contains fetal DNA, is amplified at 19,500 loci using a targeted PCR assay and sequenced using a high-throughput sequencer. Sequencing data is analyzed using Natera's proprietary NATUS algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X, and Y, thereby identifying whole chromosome abnormalities at those chromosomes, 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 that chromosome.

Being the most accurate means providing you with results you can trust. A small percentage of samples may require a second blood draw to provide more clarity. Reasons for redraw may include:

- Low fetal fraction: Samples with lower fetal fractions tend to have higher rates of redraws and higher aneuploidy rate. Pregnancies with trisomies 18 and 13, Monosomy X and maternal triploidy tend to have lower fetal fraction than euploid pregnancies.
- Insufficient sample: Panorama requires 2 tubes with 10 mL in each of the mother's blood.
- Other quality metrics.

References

For a list of complete citations please visit http://www.panoramatest.com/FactSheetReferences1.

Comprehensive DNA-Based Prenatal Screening Solutions

Natera is committed to providing expecting parents with vital information about their baby's health.

Most people do not know they are a carrier for an inherited genetic disease until they have a child with the disease. To identify a couple's potential risk of having an affected child, Natera has developed Horizon™, a carrier screening panel that includes screening for disorders recommended by experts including the American College of Medical Genetics (ACMG) and the American Congress of Obstetricians and Gynecologists (ACOG). The Horizon Carrier Screen, combined with Panorama, can be performed simultaneously as early as nine weeks gestation with a single order, or any time before or during pregnancy.

panorama™ prenatal screen

ANEUPLOIDIES

- Trisomies 21, 18 and 13
- Monosomy X
- Sex chromosome trisomies
- Triploidy / Vanishing Twin
- Fetal sex (optional)

MICRODELETION SYNDROMES

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

Note: NY State has approved Panorama's aneuploidy panel for high-risk patients and has conditionally approved the 22q11.2 microdeletion test for all patients.

Ordering Information

Panorama collection kits are provided to the clinic at no charge and can be stored on site.

To order a Panorama Prenatal Screen collection kit

CALL: 877.476.4743

OR EMAIL: customersupport@natera.com

Turnaround time: 4 - 7 business days, 5 on average

natera™ Conceive. Deliver.

natera | 201 Industrial Road, Suite 410 | San Carlos, CA 94070 | 1-877-476-4743 | Fax 1-650-730-2272

panorama™ prenatal screen

horizon™ carrier screen

spectrum™ preimplantation genetics (PGS/PGD)

anora™ miscarriage test (POC)

These tests were developed by Natera, Inc., a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA). These tests have not been cleared or approved by the U.S. Food and Drug Administration (FDA).

PAN-MD-FACT-REV1(6/24/14)