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Panorama: the next generation of NIPT

Non-invasive prenatal screen

Bangkok Cytogenetics Center

Panorama™
Next-generation NIPT
POWERED BY NATERA

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: Panorama NIPT Thailand

version 2019

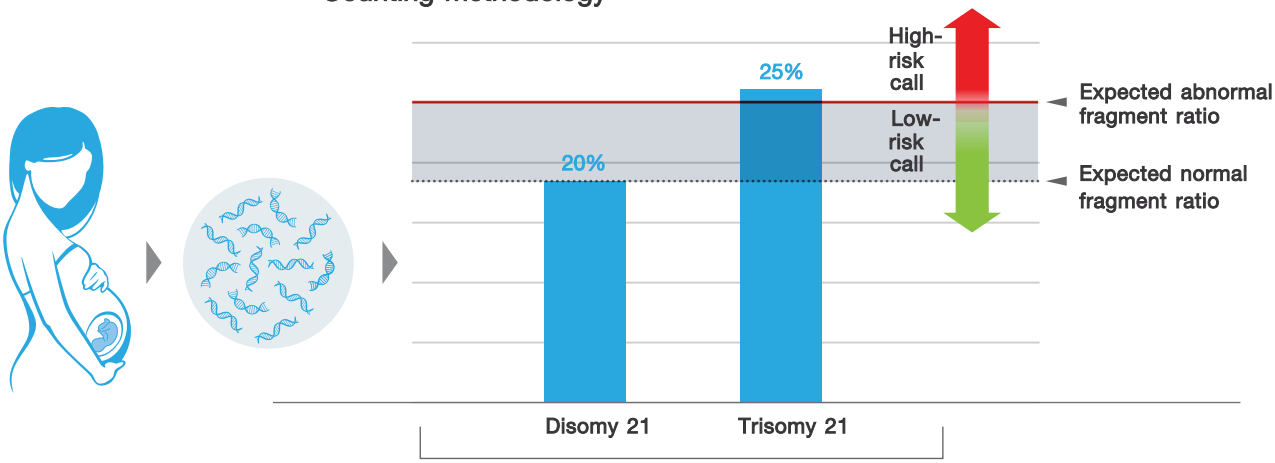
Panorama improves upon first-generation NIPTs

First-generation NIPTs use a "counting methodology" to assess risk

Laboratories that utilize whole-genome sequencing technologies (referred in this brochure as WGS-1 and WGS-2) and array-NIPT, examine fragments of conserved DNA sequences – the 99% of our DNA that makes us the same. These labs compare counts of fragments from chromosomes of interest, such as chromosome 21, against a selected reference chromosome, such as chromosome 3.

If the ratio of fragments between the chromosome of interest and the reference chromosome is determined by the lab to be out of proportion, then the lab identifies the result as "high risk"

Counting methodology



By looking at conserved DNA sequences and not distinguishing between maternal and fetal DNA, counting methodologies cannot detect triploidy, vanished twin, maternal mosaicism, and complete molar pregnancies.

Failure to identify these conditions can result in false negatives, false positives, and delayed diagnosis of conditions associated with maternal complications.

Panorama's SNP-based technology offers greater accuracy than first-generation NIPTs[1-11]

Panorama provides results with fewer false negatives, fewer false positives, and identification of maternal complications.

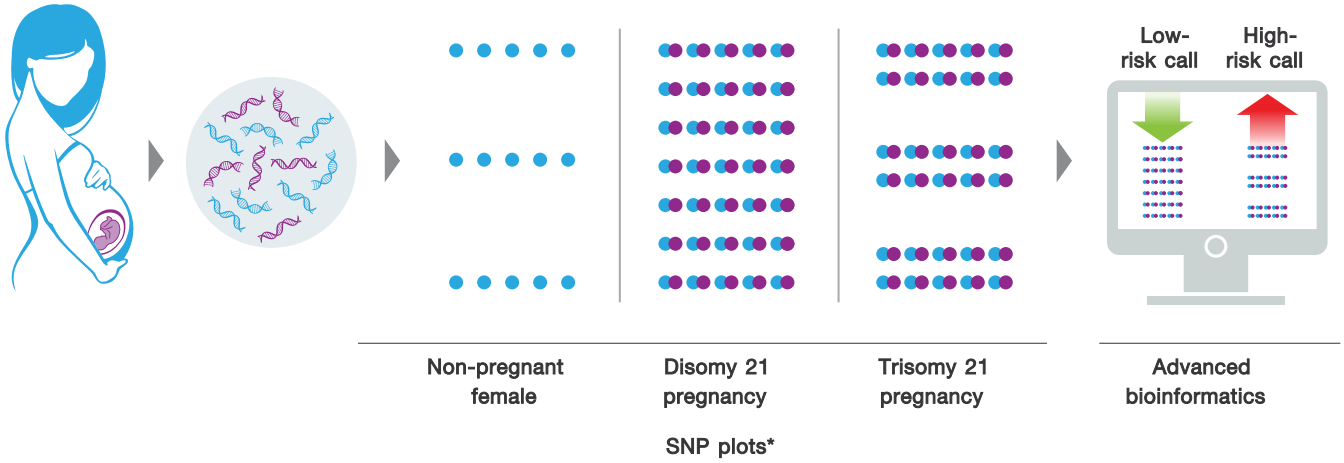
*Representation of counting methodology for illustrative purposes

Panorama is the only NIPT that can distinguish between maternal and fetal (placental) DNA

Panorama isolates single nucleotide polymorphisms (SNPs) – the 1% of our DNA that makes us different from one another.

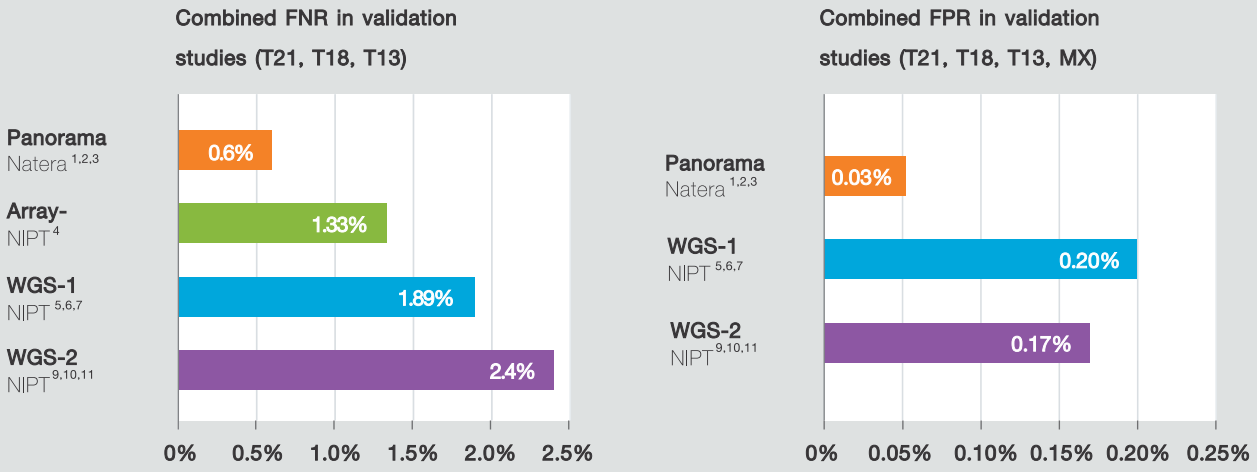
Our technology sequences targeted chromosomal regions of interest and plots SNP patterns from maternal and fetal cell-free DNA. The patterns are evaluated by our proprietary algorithm to determine if the allele patterns indicate increased risk of fetal abnormalities.

Panorama's SNP-based methodology



By distinguishing between maternal and fetal DNA, Panorama can detect triploidy, vanished twin, and complete molar pregnancies. This distinction also minimizes the chance that maternal mosaicism will lead to an incorrect result.

Compared to first-generation NIPTs, Panorama reduces both false negative rates (FNR) and false positive rates (FPR)[12-16]



Array-NIPT is excluded from the FPR chart because data on monosomy X, a leading contributor to false positives for counting methodologies, is not reported in reviewed literature.[4]

*Representation of a SNP plot for illustrative purposes

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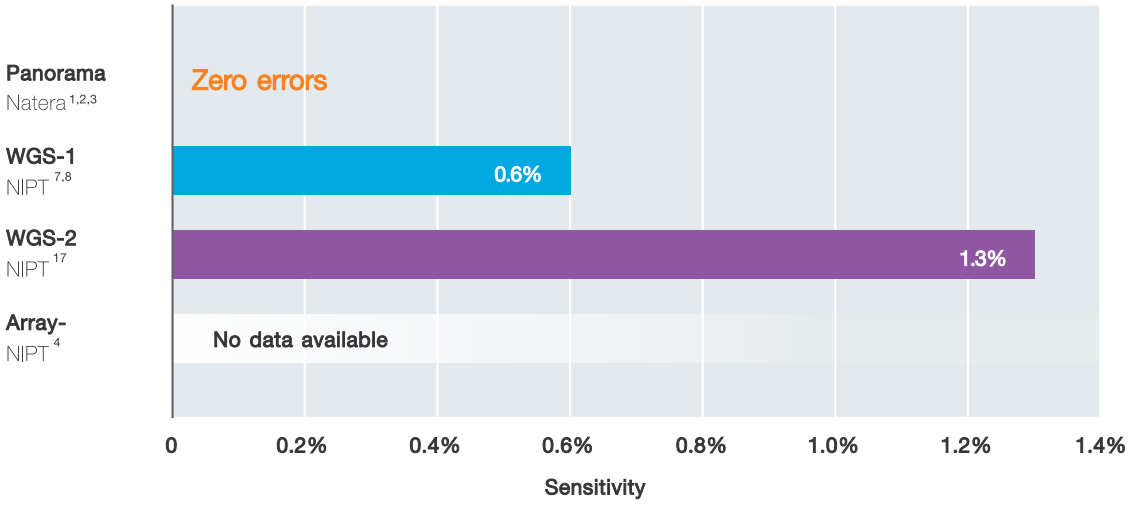
Panorama's SNP-based technology results in the highest validated fetal sex accuracy of any NIPT [1-4,8,9,17]

Panorama utilizes a specific sex-chromosome algorihm that compares SNPs from X and Y to determine the presence and copy number of Y.[18]

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

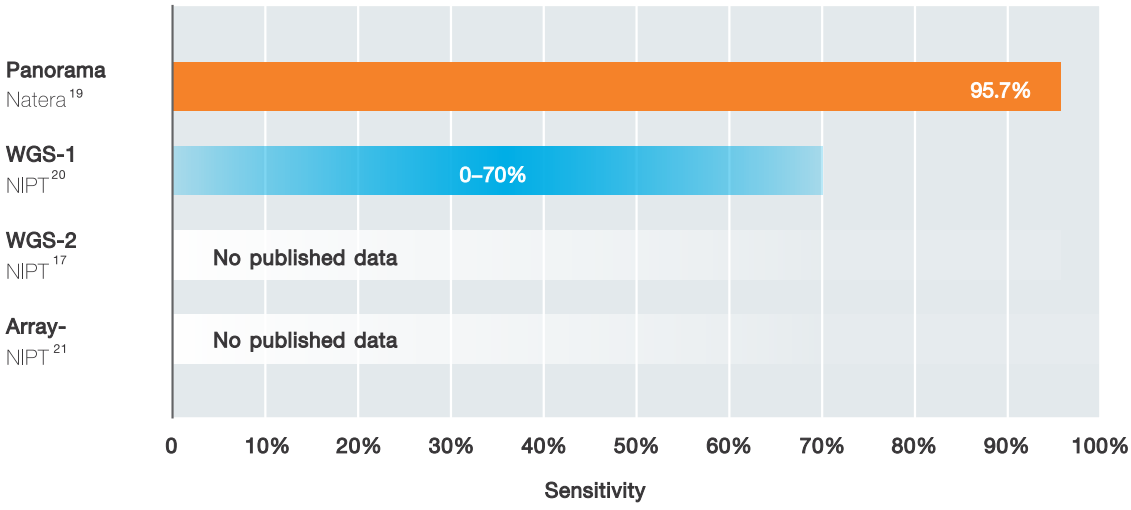
Fetal sex error rates: summary of validation studies



Panorama's SNP-based approach yields the highest commercially available sensitivity for 22q[19-21]

By evaluating unique DNA sequences within the critical region associated with 22 q11.2 deletion syndrome, Panorama has a higher detection rate than counting methodologies. First generation NIPTs count conserved DNA fragments for chromosome 22 and can overlook small deletions, like 22q.

Panorama leads the field in 22q11.2 screening sensitivity



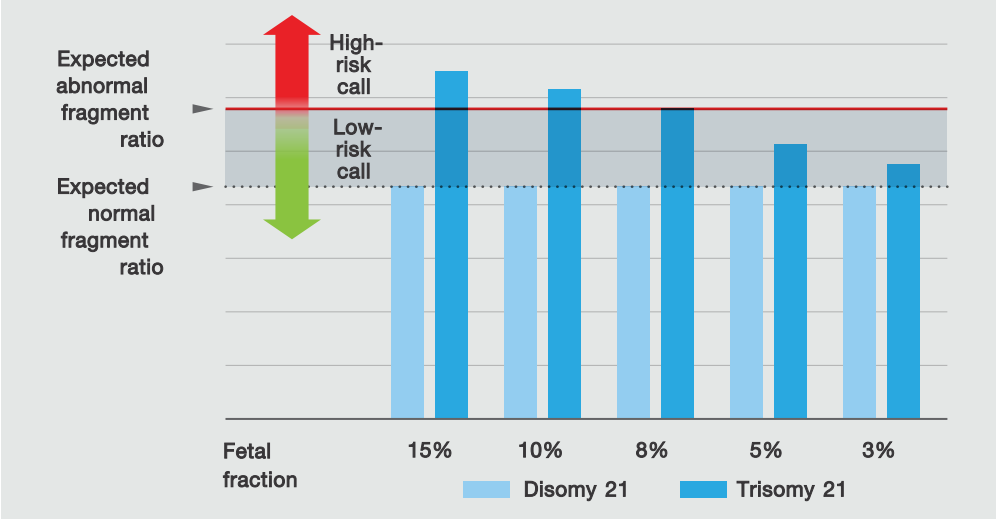
Accurate fetal fraction measurement is essential to accurate results[21]

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

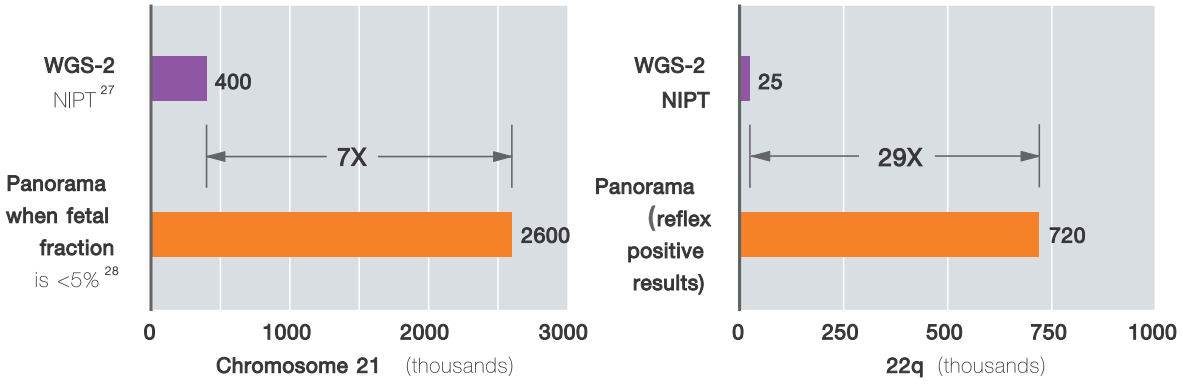
	Panorama[1,2,3]	Array-NIPT[1,2,3]	WGS-1 NIPT[5,6,7,24]	WGS-2 NIPT[9,10,11]
Method of fetal fraction measurement	13,392 SNPs	576 SNPs	Distribution of short (<150 bp) cfDNA	No data available on methodology or performance
Combined false negative rate in validation studies (Trisomies 21, 18, 13)	0.60%	1.33%	1.89%	2.40%

Counting methodologies' ability to detect abnormalities drops off below 8% fetal fraction, which can produce false negative results[25,26]



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

Panorama's proprietary algorithm incorporates fetal fraction measurement and reflexes samples with lower fetal fraction to a higher depth of read.



Are you offering Panorama to women of all ages?

NIPT is strongly supported by guidelines

The American Congress of Obstetricians and Gynecologists (ACOG), as well as the American College of Medical Genetics and Genomics (ACMG), among other societies, now acknowledges the use of NIPT for all singleton pregnancies, regardless of age or risk.[29,30]

Panorama is the only NIPT validated in high- and low-risk patients

Validation T21, T18, T13, and MX[2]		
High-risk:	Sensitivity: 98.0%	Specificity: 99.5%
Low-risk:	Sensitivity: 100%	Specificity: 100%

Professional societies recognize NIPT as a first-line screening option

ACMG American College of Medical Genetics and Genomics

"Informing all pregnant women that NIPS is the most sensitive screening option"

ACMG Position Statement, July 2016

"Data on the performance of cell-free DNA testing in the general obstetric population are now available [and]... similar to the levels previously published for the high-risk population."

ACOG/SMFM Practice Bulletin #163, May 2016

"Different scenarios... are possible, including NIPT as an alternative first-tier option.

ASHG policy, March 2015

ispd

"The following protocol [is] currently considered appropriate; cfDNA screening as a primary test offered to all pregnant women."

Position statement from the Chromosome Abnormality Screening Committee, June 2015

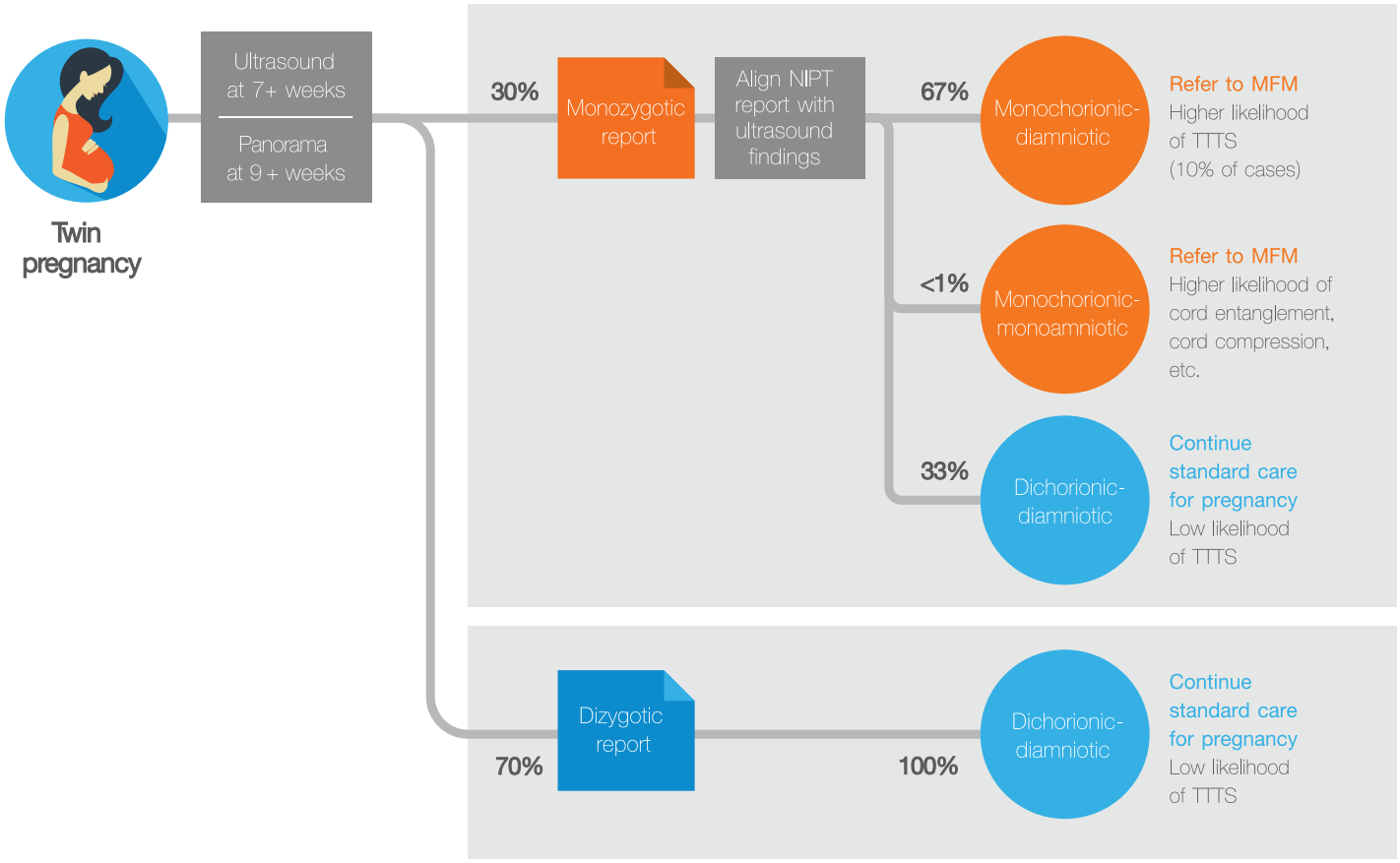
Panorama™ Next-generation NIPT

Panorama helps clinicians triage twin pregnancies effectively[2–7]

While chorionicity can be reliably detected early in a pregnancy, studies have shown that up to 19% of monochorionic pregnancies are incorrectiy classified as dichoriomic.[4]

Panorama allows clinicians to align their ultrasound findings with an early and accurate zygosity determination.

Identifying a monozygotic twin pregnancy with Panorama can prompt earlier, targeted ultrasound assessments for chorionicity and associated complications. Knowing that a twin pregnancy is dizygotic reduces concerns about TTTS.



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PAN_MD_FS_TWINS_2017_09_20_NAT-801574_INTL

Bangkok Cytogenetics Center

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
CaseFile 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™ Next-generation NIPT

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 Y : TWINS

Result	*Zygosity*	*Fetal Sex*	*Fetal Fraction(s)*
HIGH RISK for Trisomy 21	Dizygotic	♂ Male	8.3%, 8.4%
	FRATERNAL 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, even with high risk results, the fetus may be unaffected

RESULT DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[3]
Trisomy 21	High Risk	1/152	7/10
Trisomy 18	Low Risk	1/111	<1/10,000
Trisomy 13	Low Risk	1/357	<1/10,000

1. Reporting for Monosomy X, Triploidy, and microdeletion syndromes is not available for dizygotic 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 as well as analytical 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.

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.

Panorama™ Next-generation NIPT

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)
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FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
HIGH RISK for Angelman syndrome	Male	8.3%

This is a screening test only. Genetic counseling and diagnostic testing, either by microarray and UPD testing for both iso- and heterodisomy, or by methylation testing, 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, even with high risk results, the fetus may be unaffected.

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	High Risk	1/12,000	1/10
Cri-du-chat syndrome	Low Risk	1/20,000	1/57,100
Prader-Willi syndrome	Risk Unchanged	1/10,000	1/10,000

1. Excludes cases with evidence of fetal and/or placental mosaicism2. 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

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Under collaboration between faculty of Medicine Siriaj Hospital, Mahidol University and Bangkok Cytogenetics Center Company Limited.

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Patient Information

Patient Name:	
Date of Birth:	
Maternal Age at EDD:	39
Gestational Age:	13 weeks/2 days
Maternal Weight:	38.6 Kgs
Patient ID:	
Medical Record #:	N/A
Collection Kit:	5979155-2-N
Reference ID:	N/A
Accessioning ID:	
Case File ID:	

Test Information

Ordering Physician:	
Hospital/Clinic:	
Additional Reports:	N/A
Report Date:	13 Nov 2018
Samples Collected:	05 Nov 2018
Samples Received:	07 Nov 2018
	Mother Blood

FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
LOW RISK	Female	23.55%

RESULT DETAILS: ANEUPLOIDIES

Condition tested [1]	*Result*	*Risk Before Test* [2]	*Risk After Test* [3]
Trisomy 21	**Low Risk**	1/125	**<1/10,000**
Trisomy 18	Low Risk	1/330	<1/10,000
Trisomy 13	Low Risk	1/1029	<1/10,000
Monosomy X	Low Risk	1/568	<1/10,000
Triploidy	Low Risk		

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 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.

Analyzed By: Rachawalan

Rachawalan Suriyasaengsri, B.Sc.
Scientist

Approved By: N. Poungvarin

Naravat Poungvarin, M.D., Ph.D.
Head of Clinical Molecular Pathology Laboratory

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 02-690-0063, 086-306-2084 OR SEND US AN INQUIRY TO INFO@BCCGROUP-THAILAND.COM

Panorama™ Next-generation NIPT

Bangkok Cytogenetics Center

Test Panel	Panorama™ Prenatal Basic Panel (Thailand / USA)	Panorama™ Plus 22q11.2 Panel (Thailand / USA)	Panorama™ Plus Microdeletions Panel (Thailand / USA)
Method	Next generation Sequencing using SNPs Technology		
Facility Location	Thailand: Siriraj Hospital / USA: Natera, California		
Abnormality Detection	1. Aneuploidy of chromosome 13, 18, 21, X, Y 2. Triploidy	1. Aneuploidy of chromosome 13, 18, 21, X, Y* 2. Triploidy 3. 22q11.2 deletion	1. Aneuploidy of chromosome 13, 18, 21, X, Y* 2. Triploidy 3. 5 microdeletions - 22q11.2 deletion - Prader Willi Syndrome - Angelman Syndrome - Cri Du Chat Syndrome - 1p36 deletion
Minimum Gestation Age	9 weeks (Recommendation; 12 weeks)		
Sample Requirement	Maternal blood 16-20 ml in Streck tubes		
Turn Around Time	10 -14 working days		
Confirmation Test	Karyotype + QF-PCR (up to 20,000 baht)	Karyotype + Array CGH (up to 20,000 baht)	
Guarantee (False Negative)	3,500,000 THB (Trisomy 13, 18, 21)		
Twin pregnancy	USA only	USA only (Monozygotic twins)	N / A
Egg donor/ Surrogate on singleton pregnancy	USA only	N / A	N / A

*** Twin pregnancies report sex chromosome aneuploidies only for monozygotic twins**

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horizon™ ADVANCED CARRIER SCREEN | Panorama™ Next-generation NIPT | vistara SINGLE-GENE NIPT | spectrum™ PREIMPLANTATION GENETICS | anora™ MISCARRIAGE TEST (POC) | eve NEWBORN STEM CELL BANKING

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CAP accredited and CLIA certified, ISO 13485.

CAUTION: The law restricts these tests/products to sale by or on the order of a physician. Indications, contraindications, warning and instructions for use can be found in the Test/Product labeling supplied with each test/product. Information for use only in countries with applicable health authority test/product registrations.

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