Neo Test technical datasheet

Source: VeriSeq NIPT Solution v2 Package Insert (Document # 1000000078751 v02)

Juno Genetics employs VeriSeq NIPT v2 method by Illumina for the purpose of Neo tests. The clinical accuracy of the VeriSeq NIPT Solution v2 was demonstrated by Illumina by evaluating plasma samples from pregnant women with singleton and twin pregnancies. These samples underwent previous prenatal screening for fetal chromosome aneuploidies and partial deletions and duplications of 7 Mb or greater. A total of 2,335 samples were in the testing analysis set. From this set, 2,328 samples were from singleton pregnancies and seven samples were from twin pregnancies.

- Mean average maternal age: 35.08 years
- Median age: 34.95 years (25th percentile: 32.31 years; 75th percentile: 37.79 years)
- 98% of samples were from first trimester pregnancies
- Basic screen: NIPT for five chromosomes; 13, 18, 21, X and Y
- Genomewide screen: NIPT for all chromosomes, including segmental aneuploidies >7Mb

SINGLETON PREGNANCIES RESULTS:

The data shown in Table 1 corresponds to the detection of trisomies for chromosomes 21, 18 and 13 only, not including mosaic forms or other abnormalities such as partial deletions or duplications. Table 2 lists all anomalies detectable by VeriSeq NIPT solution v2 for all chromosomes (chromosomes 1 to 22, X & Y).

Table 1. Sensitivity and Specificity of the VeriSeq NIPT Solution v2 for detecting Trisomy 21, 18, & 13.

CLINICAL PERFORMANCE DATA	Trisomy 21	Trisomy 18	Trisomy 13
Sensitivity	> 99.9% (130/130)	> 99.9% (41/41)	> 99.9% (26/26)
2-sided 95% CI	97.1%, 100%	91.4%, 100%	87.1%, 100%
Specificity	99.90% (1982/1984)	99.90% (1995/1997)	99.90% (2000/2002)
2-sided 95% CI	99.63%, 99.97%	99.64%, 99.97%	99.64%, 99.97%

Table 2. Sensitivity and Specificity of the VeriSeq NIPT Solution v2 (Genomewide Screen) for detecting various chromosomal anomalies (including trisomies, monosomies, and partial deletions or duplications of 7 Mb or greater) for any chromosome are provided in the table below.

CLINICAL PERFORMANCE DATA	Rare Autosomal Aneuploidy (RAA)*	Partial deletions and duplications (>7Mb)	OVERALL PERFORMANCE FOR ANY ANEUPLOIDY
Sensitivity	96.4% (27/28)	74.1% (20/27)	95.5% (318/333)
2-sided 95% CI	82.3%, 99.4%	55.3%, 86.8%	92.7%, 97.3%
Specificity	99.80% (2001/2005)	99.80% (2000/2004)	99.34% (1954/1967)
2-sided 95% CI	99.49%, 99.92%	99.49%, 99.92%	98.87%, 99.61%

**These are trisomies and monosomies of chromosomes 1 – 12, 14 – 17, 19, 20 and 22 as well as monosomies of chromosomes 13, 18 and 21.*

Table 3. Concordance of VeriSeq NIPT Solution v2 results for fetal sex

	Newborn Physical Exam Outcome		Cytogenetic Results					
Percent Concordant	Female	Male	XX	XY	X0	XXX	XXY	XYY
	100%	100%	100%	100%	90.50%	100%	100%	91.70%

TWIN PREGNANCIES RESULTS:

Table 4. Estimates for Trisomy 21, 18, and 13 in Simulated Population of Twin Pregnancies

CLINICAL PERFORMANCE DATA	Trisomy 21	Trisomy 18	Trisomy 13	Presence of Y chromosome
Sensitivity	96.4%	95.7%	93.6%	> 99.9%
2-sided 95% CI	(86.4%, 98.9%)	(68.3%, 99.4%)	(64.1%, 98.9%)	(99.9%, > 99.9%)
Specificity	99.9%	> 99.9%	> 99.9%	> 99.9%
2-sided 95% CI	(99.8%, > 99.9%)	(99.9%, > 99.9%)	(99.9%, > 99.9%)	(99.7%, > 99.9%)

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Positive Predictive Value and Negative Predictive Value of the VeriSeq NIPT Solution v2

Positive predictive value (PPV) and negative predictive value (NPV) of the test provide information regarding the ability of the test to inform clinical decisions based on test sensitivity, specificity, and pretest probability that a fetus is affected by an aneuploidy (prevalence). The PPV and NPV depend on prevalence, which can vary for these aneuploidies across different subject populations.

Table 5. Trisomy 21 Prevalence, PPV and NPV in Basic Screen (Excluding known mosaics)

Prevalence (%)	PPV (%)	NPV (%)
0.05	33.17	>99.99
0.10	49.82	>99.99
0.20	66.53	>99.99
0.50	83.29	>99.99
1.00	90.93	>99.99
1.50	93.79	>99.99
2.00	95.29	>99.99

Table 6. Trisomy 18 Prevalence, PPV and NPV in Basic Screen (Excluding known mosaics)

Prevalence (%)	PPV (%)	NPV (%)
0.03	23.06	>99.99
0.05	33.31	>99.99
0.10	49.99	>99.99
0.20	66.68	>99.99
0.30	75.03	>99.99
0.40	80.04	>99.99
0.50	83.38	>99.99

Table 7. Trisomy 13 Prevalence, PPV and NPV in Basic Screen (Excluding known mosaics)

Prevalence (%)	PPV (%)	NPV (%)
0.01	9.1	>99.99
0.02	16.68	>99.99
0.05	33.37	>99.99
0.10	50.05	>99.99
0.20	66.73	>99.99

Table 8. Any Anomaly Prevalence, PPV and NPV in Genomewide Screen (Including known mosaics)

Prevalence (%)	PPV (%)	NPV (%)
0.01	1.42	>99.99
0.02	2.81	>99.99
0.05	6.74	>99.99
0.10	12.64	>99.99
0.20	22.45	99.99
0.50	42.07	99.98
1.00	59.34	99.95
1.50	68.75	99.93
2.00	74.68	99.91

IMPORTANT NOTES:

- The Neo test is not intended to detect polyploidy, such as triploidy.
- The test cannot detect balanced chromosome rearrangements.
- The results of the test can be confounded by certain maternal and fetal factors including but not limited to recent maternal blood transfusion, maternal organ or stem cell transplant, maternal mosaicism, the existence of a maternal tumor, the use of low molecular weight heparin treatments, undeclared multiple gestation (two or more fetuses), fetal age less than 10 weeks, nonviable (vanishing) twin or fetoplacental mosaicism.
- The test is not validated or intended for higher order multiple pregnancies (triplets, quadruplets, etc).

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