NEXT BIOSCIENCES

TriScreen
Non-Invasive Prenatal Test (NIPT)
Product Specification Sheet

NG-MAR-NIPT-INF-002-REV-002 | 2023.04.01

What is NIPT?

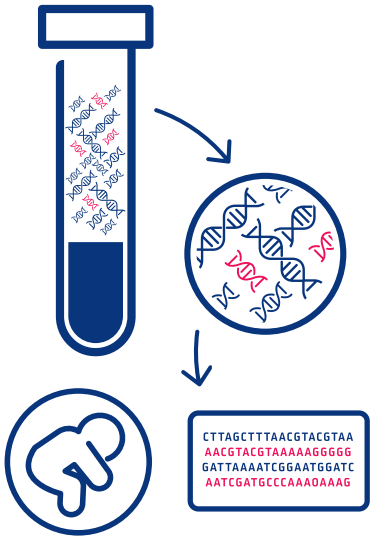
NIPT analyses cell-free DNA (cfDNA) from a maternal blood sample (which contains a mixture of placental and maternal cfDNA) to screen for common chromosomal aneuploidies including trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome).

Genome-wide, NIPT screening allows not only for the detection of common chromosomal aneuploidies, but also enables the identification of rare autosomal aneuploidies (RAAs), as well as partial deletions and duplications that are ≥7 Mb in size.

The American College of Obstetricians and Gynecologists (ACOG) and International Society of Prenatal Diagnosis (ISPD), along with other professional societies, have stated that NIPT is an available screening option for all pregnant women.[1,2]

Fetal DNA in maternal blood

- Maternal cfDNA
- Fetal (placental) cfDNA



NIPT vs. traditional serum screening

- Offers the highest reported detection rate for Down syndrome[2]
- Offers the lowest reported false positive rate for Down syndrome[3]
- Offers the broadest screening window (performed as early as 10 weeks gestation until term)[2]

Benefits of NIPT?

- Non-invasive with no risk of miscarriage
- High detection rates for chromosomes tested
- High sensitivity and specificity compared to traditional serum screening

Limitations of NIPT

- NIPT is a screening test, not a diagnostic test and must be followed up with an invasive test if a definitive diagnosis is needed.
- In rare instances, results may represent a maternal or placental condition, rather than a fetal condition

Test options

- **TriScreen (Standard Panel)** - T21, T18, T13
- **TriScreen + (All Chromosomes)** - Fetal DNA in maternal blood and segmental deletions and duplications >7Mb
- **Optionally reported** - information on the status of fetal sex chromosomes and certain sex chromosome aneuploidies
- **Microdeletions** - sent to Illumina. Extra costs and longer turnaround time

TriScreen can be performed on:

- Singleton pregnancies
- Twin pregnancies
- Donor pregnancies
- IVF pregnancies (from 8 weeks post implantation)
- Surrogate pregnancies

Indications

All pregnant women can be offered the option of NIPT

1. **Patients at high risk for aneuploidy due to:**
   - Maternal age-related risks
   - Increased risk on maternal-serum screening
   - Abnormal ultrasound finding(s) in patients who decline invasive testing
   - History suggestive of increased risk for T21, T18, T13, other autosomal aneupoidy, or sex chromosome anomalies
   - Parental translocation involving one of the tested chromosomes (depending on size)
2. **Patients at low risk for aneuploidy**

Indications for All Chromosome Test

- History of a pregnancy with chromosomal anomalies
- Abnormal ultrasound findings and patient wants to avoid invasive test
- Known parental translocation (depending on size)
- Patients who want more detailed information and have had a genetic counselling appointment to understand the limitations of the test, and the possibility of false positives and negatives

Anyone considering genome wide testing should be strongly advised to have an appointment with a genetic counsellor/detailed discussion with their obstetrician (regardless of the indication).

Technology

TriScreen uses whole-genome sequencing with next-generation sequencing (NGS) technology to analyse cell-free DNA (cfDNA) fragments across the whole genome, which has proven advantages over other NIPT methodologies such as targeted sequencing and array-based methods. Test failure rates are substantially lower with whole-genome sequencing versus other methodologies.[9 - 12]

With its high levels of sensitivity and accuracy, NGS produces the data quality needed for reliable analysis of the trace amounts of cfDNA found circulating within blood plasma.

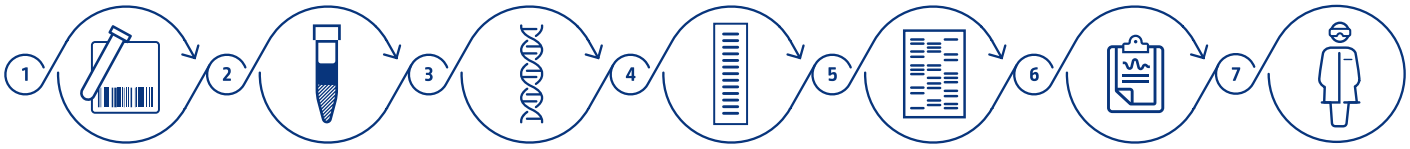
Performance Metrics

Chromosome	N	Sensitivity	95% CI	Specificity	95% CI
Trisomy 21	2 236	99.9% (130/130)	97.1 - 100.0	99.90% (1982/1984)	99.63 - 99.97
Trisomy 18	2 236	99.9% (41/41)	97.4 - 100.0	99.9% (1995/1997)	99.64 - 99.97
Trisomy 13	2 236	99.9% (14/16)	87.1 - 100.0	99.9% (2000/2002)	99.64 - 99.97
RAA**	2 300	96.4% (27/28)	82.3 - 99.4	99.8% (2001/2005)	99.49 - 99.92
CNV ≥ 7Mb	2 300	74.1% (20/27)	55.3 - 86.8	99.8% (2000/2004)	99.49 - 99.92
Any anomaly***	2 300	95.5% (318/333)	92.7 - 97.3	99.34% (1954/1967)	98.87 - 99.61

* Data from VeriSeq NIPT Solutions V2 package insert
** RAA excludes chomosomes 21, 18, 13
*** Includes sex chromosomes anomalies from genome wide screen

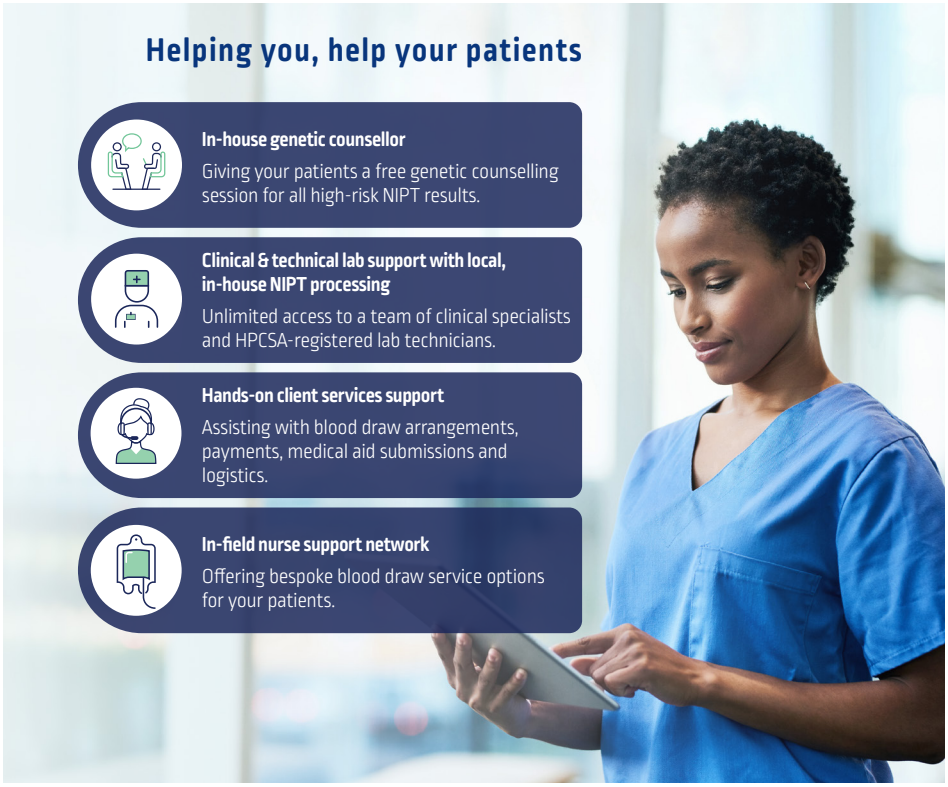
Key:
N: Sample size
CI: Confidence interval
RAA: Rare autosomal aneuploidy
CNV: Copy number variation

Methodology



Sample receipt and barcoding | Plasma isolation | Cell-free DNA extraction | Library preparation | Next generation sequencing | Analysis | Results and report generation

Helping you, help your patients



In-house genetic counsellor
Giving your patients a free genetic counselling session for all high-risk NIPT results.

Clinical & technical lab support with local, in-house NIPT processing
Unlimited access to a team of clinical specialists and HPCSA-registered lab technicians.

Hands-on client services support
Assisting with blood draw arrangements, payments, medical aid submissions and logistics.

In-field nurse support network
Offering bespoke blood draw service options for your patients.

How to order the NIPT Test

1. Complete the TriScreen **Test Requisition Form**
2. **Scan the TRF** and send it to our Client Services team: **triscreen@nextbio.co.za** (if your patient requires medical aid approval, please send the supporting documents with the TRF).
3. The Client Services Team **will be in contact** with your patient to make the necessary arrangements for the blood draw.
4. **Pre-test counselling video** is sent to your patient to watch.
5. **Next Biosciences bills the medical aid** if preapproved for reimbursement from risk. If not approved, the patient is responsible for settling with Next Biosciences directly.
6. Turnaround time for results is **7-10 working days** from the date of the blood draw. Results will be released to the requesting HCP.
7. **A genetic counselling session** is available to patients with a positive result, free of charge.

References
1. Benn P, Borrell A, Chiu R, et al. Position statement from the Chromosome Abnormality Screening Committee on behalf of the board of the International Society for Prenatal Diagnosis. Prenat Diagn. 2015;35(8):725-734.
2. American College of Obstetricians and Gynecologists: Screening for fetal aneuploidy. Obstet Gynecol. 2016;127(5):e123-137.
3. Bianchi DW, Parker RL, Wentworth J, et al. DNA sequencing versus standard prenatal aneuploidy screening. N Engl J Med. 2014;370(9):799-808.
4. Data calculation on file. Illumina, Inc. 2017.
5. VeriSeq NIPT Solution Package Insert
6. Data calculation on file. Illumina, Inc. 2018
7. VeriSeq NIPT Solution v2 Package Insert
8. Committee Opinion No. 640: Cell-free DNA Screening for Fetal Aneuploidy. Obstet Gynecol. 2015;126(3):e31-37.
9. Norton ME, Jacobsson B, Swamy GK, et al. Cell-free DNA analysis for noninvasive examination of trisomy. N Engl J Med. 2015;372(17):1589-1597.
10. Taneja PA, Snyder HL, de Feo E, et al. Noninvasive prenatal testing in the general obstetric population: clinical performance and counseling considerations in over 85,000 cases. Prenat Diagn. 2016;36(3):237-243.
11. McCullough RM, Almasri EA, Guan X, et al. Non-invasive prenatal chromosomal aneuploidy testing-clinical experience: 100,000 clinical samples. PLoS One. 2014;9(10):e109173.
12. Dar P, Curnow KJ, Gross SJ, et al. Clinical experience and follow-up with large scale single-nucleotide polymorphism-based noninvasive prenatal aneuploidy testing. Am J Obstet Gynecol. 2014; 211(5): 527e1-527e17.

POWERED BY illumina®