NEXT BIOSCIENCES

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

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What is NIPT?

NIPT analyses cell-free DNA (cfDNA) from 10 weeks in 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) known as the **TriScreen (standard panel).**

NIPT screening allows for the detection of common chromosomal aneuploidies, and enables the identification of rare autosomal aneuploidies (RAAs), as well as partial deletions and duplications that are ≥7 Mb in size, **Genome-wide (TriScreen+).**

Next Biosciences offers Standard panel, Genome-wide NIPT and full microdeletion panel testing using Illumina NGS technology. Alternatively, 22q11.2 (DiGeorge syndrome), the most common microdeletion, as well as Fetal RhD can be added to the standard panel alone.

The **Fetal RhD and 22q11. 2** test is provided in collaboration with BilliontoOne utilising UNITY Next Generation Sequencing (NGS) coupled with QCTTM technology (sent to the USA for testing; extra costs and longer turnaround times apply). Alternatively, **Fetal RhD** can be done as a standalone test via PCR amplification in RhD exon four with high detection rates.[1]

Why NIPT?

According to the International Society for Prenatal Diagnosis **(ISPD)** position statement from 2023, non-invasive prenatal testing is a highly sensitive and specific screening test for trisomy's 13, 18, and 21, which can be implemented as a first line screening test for all pregnant women or as a contingent test in people with a higher chance of fetal aneuploidy on prior screening.[2]

Furthermore the American College of Medical Genetics **(ACMG)** recommends NIPT for all pregnant women over traditional screening for common trisomy's (in singleton and twin pregnancies).[3]

Lastly, the American College of Obstetricians and Gynecologists **(ACOG)** and the Society for Maternal-Fetal Medicine **(SMFM)** endorse NIPT as having the highest detection rate and lowest false positive rate for the common aneuploidies regardless of maternal age or baseline risk, of all screening options.[4]

ispd International Society for Prenatal Diagnosis · ACMG American College of Medical Genetics and Genomics · ACOG · Society for Maternal-Fetal Medicine

TriScreen can be performed on:

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

Benefits of TriScreen:

- Non-invasive with no risk of miscarriage
- High detection rates for chromosomes tested
- High sensitivity and specificity compared to traditional serum screening
- In-house genetic counsellor: Free session with every high-risk result
- In-field nurse support, offering bespoke blood draw service

Limitations of NIPT:

- NIPT tests cell free DNA shed from the placenta
- In rare instances, results may represent a maternal or placental condition, rather than a fetal condition due to mosaicism
- NIPT is a screening test, not a diagnostic test and high risk results must be followed up with an invasive test if a definitive diagnosis is needed

Performance metrics

Chromosome	Sensitivity	95% CI	Specificity	95% CI
Trisomy 21, 18, 13*	99.9%	97.1 - 100.0	99.9%	99.6 - 99.9
RAA**	96.4%	82.3 - 99.4	99.8%	99.49 - 99.92
CNV ≥ 7Mb*	74.1%	55.3 - 86.8	99.8%	99.49 - 99.92
Any anomaly***	95.5%	92.7 - 97.3	99.34%	98.87 - 99.61
Fetal RhD**	99.9%	99 – 100.0	99.9%	99 – 100
22q11.2**	95%		99.9%	

*Data from VeriSeq NIPT Solutions V2 package insert.[5]
**Unity Fetal™ NIPT6/UNITY Aneuploidy NIPT[6,7]

Key:
N: Sample size
CI: Confidence interval
RAA: Rare autosomal aneuploidy excludes chromosomes 21, 18, 13
CNV: Copy number variation
Any anomaly: Includes sex chromosomes anomalies from genome wide screen

TriScreen test options

TriScreen (standard panel) - T21, T18, T13 & XY

Indications for Standard Panel Testing
- Advanced maternal age
- Increased risk on maternal-serum screening
- Abnormal ultrasound finding(s)
- Previous pregnancy affected by chromosomal aneuploidy
- Patients at low risk for aneuploidy
- Testing due to patient concern or anxiety

TriScreen+ (genome-wide) - 1- 23 & XY including segmental deletions and duplications >7Mb

Additional indications for genome-wide testing:
- Known parental translocation (depending on size)
- Patient request due to patient concern or anxiety

TriScreen/ TriScreen+ including microdeletions

22q11 deletion (DiGeorge); 15q11 deletion (Angelman/ Prader-Willi); 1p36 deletion; 4p- (Wolf-Hirschhorn); 5p- (Cri-du-chat).

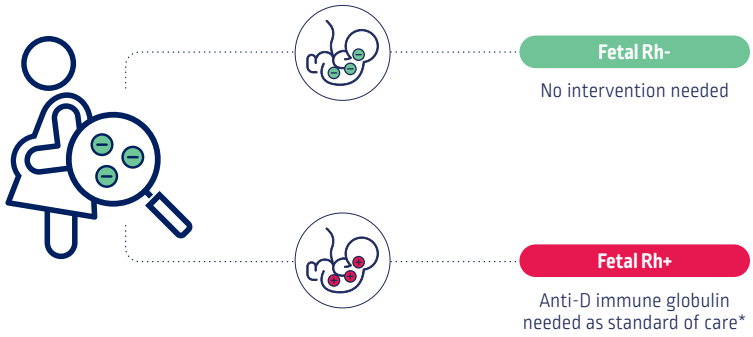
Additional indications for microdeletion testing:
- Family history of microdeletions

TriScreen & Rhesus*- Chromosome 21, 18, 13, XY, and Fetal RhD OR Standalone Fetal RhD - PCR amplification

Rhesus NIPT enables early detection of fetal D antigen, providing crucial information about fetal RhD status. Identifying RhD status early in pregnancy helps determine the need to administer anti-D immunoglobulin (RhoGAM) in RhD-negative pregnant patients. Approximately 40% of RhD-negative patients carry RhD-negative fetuses and may not require anti-D immunoglobulin.[8] This approach can streamline the management of up to 65% of alloimmunised patients.[9]

Indications for Rhesus testing:
- Rhesus negative pregnant patients
- Alloimmunised Rh-negative Mothers (Rh- mothers who test positive for anti-D antibodies)

Benefits
- Provides relief and reassurance
- Minimises need for paternal antibody screen
- Minimises the need for anti-D immunoglobulin treatment during pregancy



TriScreen & 22q11.2* - Chromosome 21, 18, 13, XY, and 22q11.2 microdeletion

22q11.2 deletion syndrome/DiGeorge syndrome/velocardiofacial syndrome, is the most common microdeletion of up to three megabases on chromosome 22. This abnormality is not associated with maternal age and has an incidence of 1 in 4 000 in the general population.[10] Early diagnosis of 22q11.2 is associated with better outcomes for affected individuals.[11]

Clinical features:
- Congenital heart defects
- Cleft palate
- Renal abnormalities
- Intrauterine growth restriction
- Developmental delay
- Immunodeficiency
- Behavioural and psychiatric disorders[10]

Indications for 22q11.2 testing:
- Previous child with a 22q11.2
- Affected parent with a 22q11.2 (50% risk of transmission[12])
- Ultrasound anomaly of a conotruncal cardiac defect
- Other ultrasound anomalies

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*Requires 2X blood tubes of blood and may be subject to longer TAT. **The positive predictive value (PPV) for 22q11.2 deletion syndrome ranges from 40-50%.[12] In other words, 1 in 2 results will be a false positive. Diagnostic testing is required to confirm high risk results.**

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