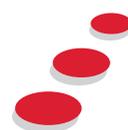




**Generation**<sup>®</sup>

a new *era* in prenatal testing

MEDICAL PRACTITIONER FACT SHEET



Abbott Pathology

# What is **Generation**<sup>®</sup> ?

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**Non-Invasive Prenatal Testing (NIPT) represents a major advance in screening and risk assessment for chromosomal abnormalities.**

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In January 2016, the UK National Screening Committee recommended systematic screening of all high risk pregnancies in the UK by NIPT<sup>1,2</sup>. In addition, clinical best practice guidelines from Australian and international medical societies recommend that all pregnant women, regardless of risk status, be offered the opportunity for discussion and choice regarding NIPT and other available prenatal screening and diagnostic tests<sup>3,4,5</sup>.

**Generation**<sup>®</sup> is a highly efficient, accurate, non-invasive prenatal screening test, based on Whole Genome Sequencing (“WGS”) with proprietary algorithms, that analyses circulating cell-free fetal DNA from a maternal blood sample from as early as 10 weeks gestation.

The clinical utility and benefit of the **Generation**<sup>®</sup> test has been demonstrated in all pregnant women – regardless of age or risk category – in numerous publications, including studies in the New England Journal of Medicine, as well as reports with cohorts of over 34,000 patients<sup>6,7,8,9</sup>.



# The benefits of whole genome sequencing

WGS provides precise counts across the genome

## BENEFITS of Generation®

- Low assay failure rates (<1%)
- Ability to add new content to test menu



Targeted sequencing is limited to few chromosomes and loci

## DRAWBACKS of this method:

- High assay failure rates (up to 12%)
- Limited ability to add new content without changing assay



Microarray has a lower resolution

## DRAWBACKS of this method:

- Array NIPT unproven with few publications and no independent replication
- High sample failure – likely requires high fetal fraction (FF) to accurately call
- Late term – High FF means late term testing



## Generation® has the lowest reported test failure rate

Test failures matter in NIPT, as they increase the risk of false negative and false positive results. There is the potential to increase false negative results if no action is taken following a test failure. A higher rate of aneuploidy in test failure samples also means that there is potentially increased invasive test utilisation for those returning a “high risk” result with other testing modalities.

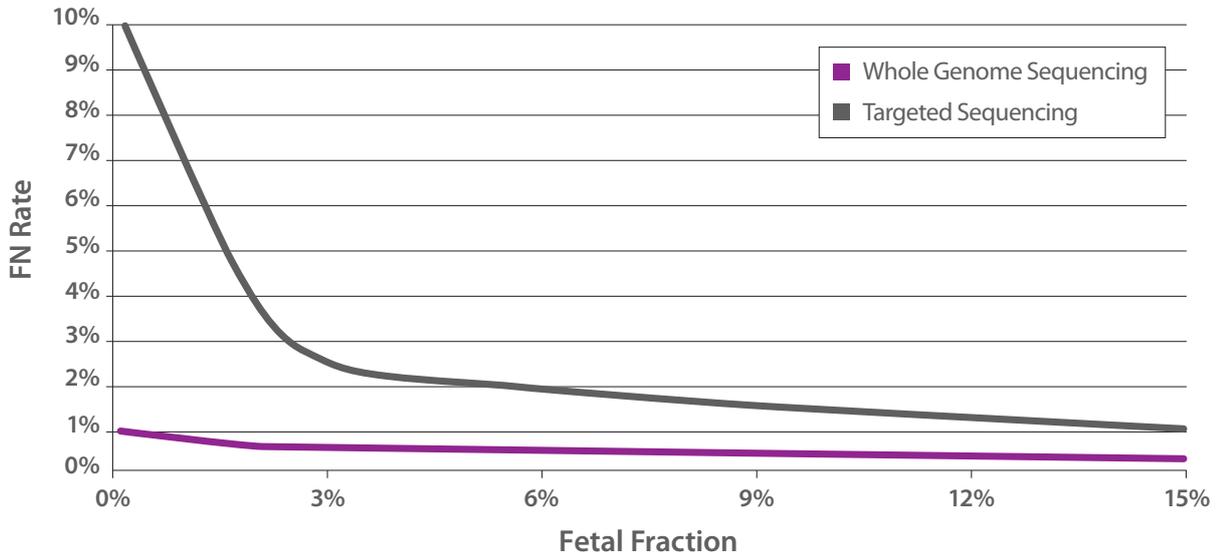
Test failures also lead to increased turnaround times and clinician visits, with high failure rates demonstrated for redraws from these patients<sup>12</sup>.



# The science of deeper sequencing

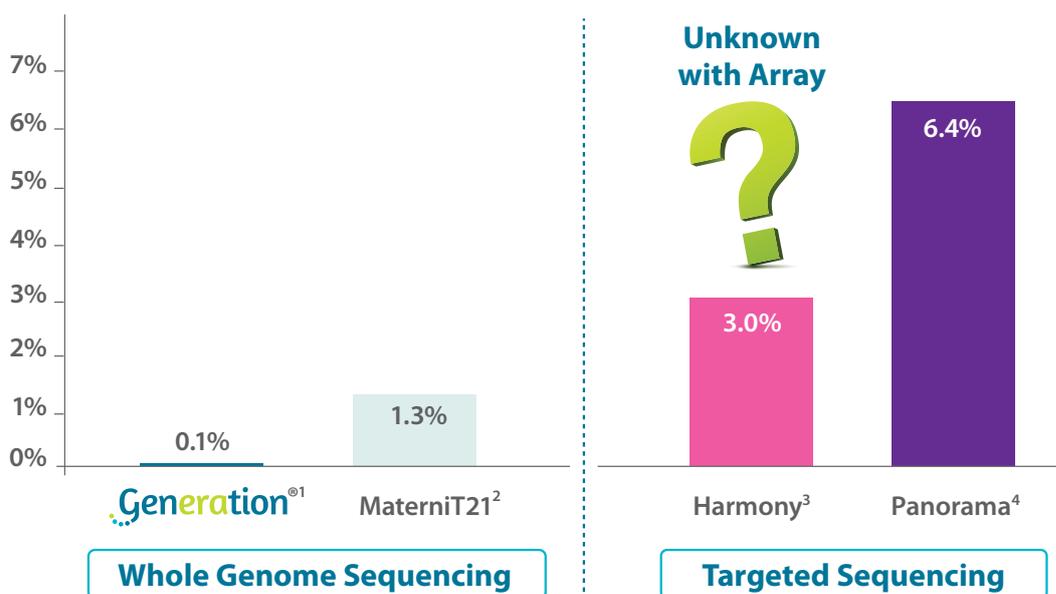
The **Generation**<sup>®</sup> NIPT analyses 28 million reads from sequencing data across the genome, enhancing the precision and accuracy of the test results. In addition, deep whole genome sequencing allows for accurate detection of sub-chromosomal abnormalities (SCA)<sup>10,11</sup>.

Unlike other tests that use restricted sequencing techniques, the whole genome sequencing approach generates rich and comprehensive results with more than 99% accuracy for trisomies 21, 18 and 13.



Data adapted from: Rava PP, Srinivasan A, Sehnert AJ, Bianchi DW. Circulating fetal cell-free DNA fractions differ in autosomal aneuploidies and monosomy X. Clin Chem. 2014;60:243–250

## Generation<sup>®</sup> minimises test failures



1. Taneja et al. Prenatal diagnosis, Dec 2015 2. McCullough RM et al. PLoS One. 2014 3. Norton ME, et al. New Engl J Med 2015 4. Dar, et al. Am J Obstet Gynecol. 2014

# What does the Generation® NIPT test for?

The Generation® NIPT screens for the most commonly seen and tested chromosomal anomalies, including trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), trisomy 13 (Patau syndrome) and Sex Chromosome Aneuploidies.

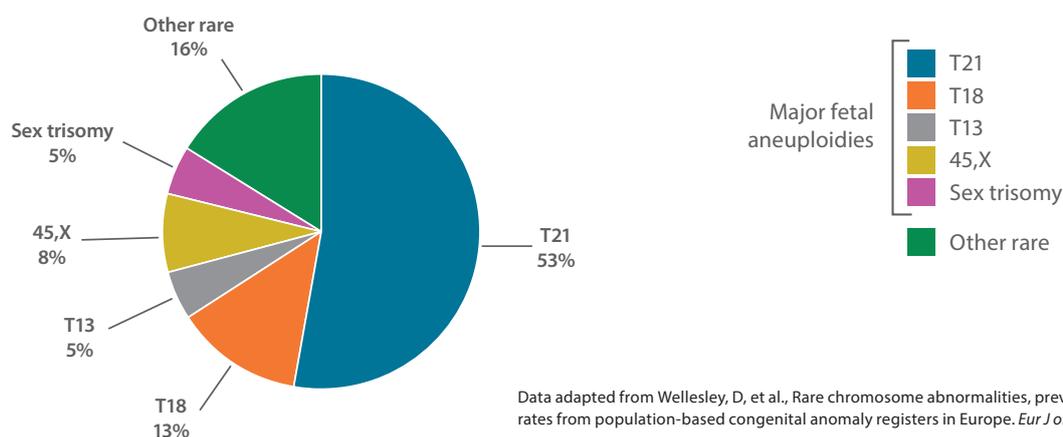
If Generation® Plus is requested, the following more rarely occurring genetic syndromes are also tested for:

- ✓ **Trisomy 9\***, which is caused by an extra copy of chromosome 9. Almost all pregnancies with trisomy 9 end in first trimester miscarriage. Pregnancies with partial trisomy 9 may survive until term, but typically have significant birth defects and intellectual disabilities.
- ✓ **Trisomy 16\***, which is caused by an extra copy of chromosome 16. Trisomy 16 is one of the most common causes of miscarriage. Pregnancies with partial trisomy 16 may survive until term, but are at increased risk for pregnancy complications and often have significant birth defects and intellectual disabilities.
- ✓ **Common microdeletions\***, involving losses and gains of partial chromosomal segments. Some of the common microdeletions which can be detected by the Generation® test include:
  - DiGeorge syndrome (22q11.2 deletion syndrome)**, which is commonly associated with heart defects, cleft palate, immune system disorders and intellectual disabilities.
  - Angelman syndrome**, which is commonly associated with significant developmental delay and learning disabilities, seizures and hyperactivity.
  - Prader-Willi syndrome**, which is commonly associated with mild to moderate intellectual disabilities, poor muscle tone and feeding difficulties in infancy that progresses to behaviour issues and compulsive over-eating in childhood.
  - Wolf-Hirschhorn syndrome**, which is associated with intellectual disability, characteristic facial features, seizures and delayed growth and development.
  - Cri-du-chat syndrome**, which is associated with intellectual disability, developmental delays, characteristic facial features and a high-pitched, cat-like cry in newborns.

\* This testing will incur additional costs. It is highly recommended that testing for microdeletion syndromes be accompanied by specialised genetic counselling.

The **Generation®** and **Generation® Plus** NIPT does **NOT** test for any genetic conditions not listed above, such as rarer chromosome abnormalities, or family specific mutations (such as cystic fibrosis). Testing for these conditions may be available by invasive methods. Please contact us if you require further information about this. Non-genetic conditions (such as neural tube defects) are similarly not tested for by NIPT.

## Prenatal prevalence of reported chromosomal abnormalities



# What are the performance characteristics for Generation® NIPT?

All screening tests carry a false positive and false negative rate. The **Generation®** NIPT provides highly accurate, near diagnostic information for the most common chromosomal abnormalities <sup>6,7,13</sup>

	Observed Sensitivity	Observed Specificity
Trisomy 21	99.1%	99.9%
Trisomy 18	98.3%	99.9%
Trisomy 13	98.2%	99.9%
Monosomy X	95.0%	99.0%
XX	97.6%	99.2%
XY	99.1%	98.9%

## Who should be offered the Generation® NIPT test?

Numerous studies have conclusively demonstrated the benefits for NIPT in women with a high risk pregnancy, including:

- ✓ Women aged over 35
- ✓ Women with abnormal first trimester combined biochemical and ultrasound findings
- ✓ Women with a family history of chromosomal abnormalities
- ✓ Women with a high risk for invasive testing (e.g. IVF)

In addition, there is significant evidence to suggest that women in a normal risk population could also benefit from NIPT, particularly for peace of mind.

Although serum biochemical screening with ultrasound is not as accurate as NIPT, patients should still be offered these tests as they are complementary tests which detect a larger range of abnormalities – including neural tube defects and non-genetic abnormalities. NIPT, biochemical testing and ultrasound testing measure different things; the genetic code versus biochemical function and fetal anatomy respectively.

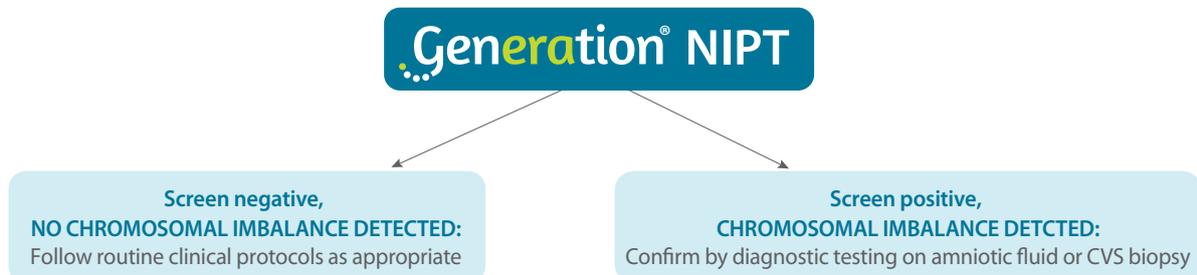
**Generation®** NIPT is a new and powerful investigative tool. Pregnancy is an important time for mothers and their fetuses, with tests, results, and recommendations carrying major clinical implications. Before proceeding with testing, it is important that all clinicians understand the purpose and performance of this test, and how to appropriately explain the results to their patients. We require that patients provide written consent ensuring that these issues have been discussed and understood by the patient and clinician.

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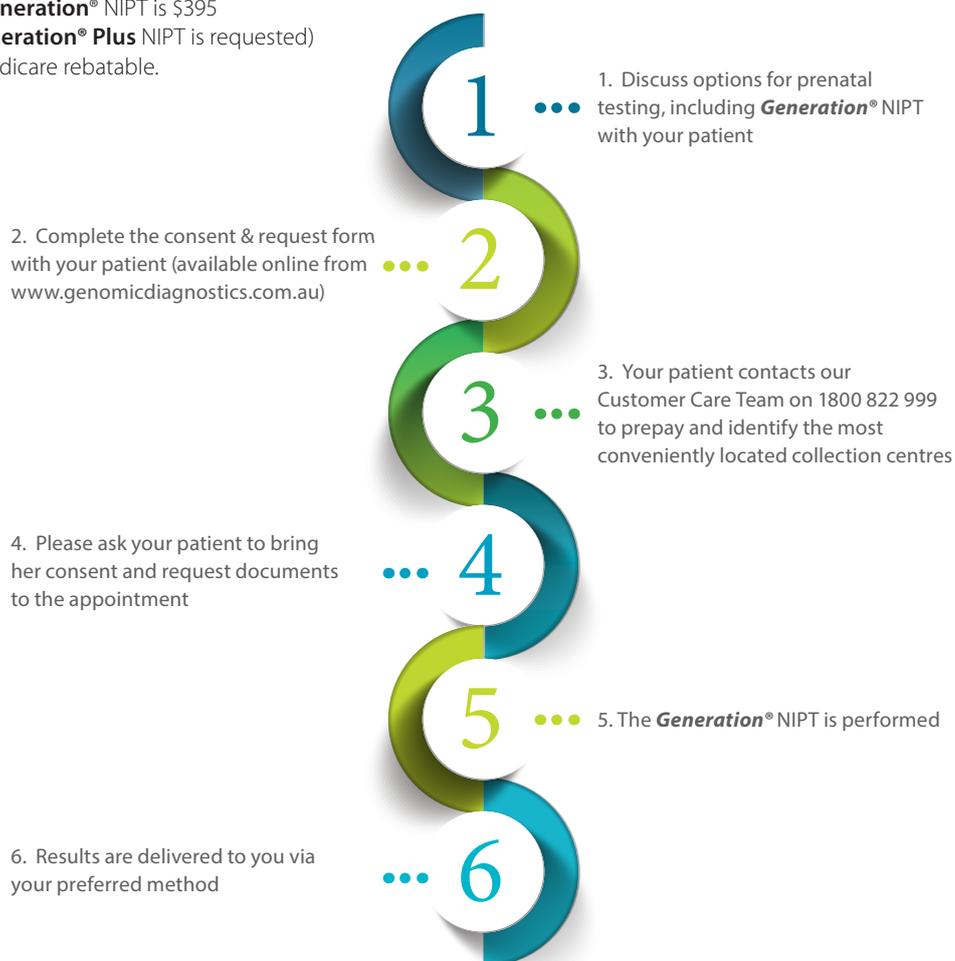
# Appropriate follow up after NIPT

NIPT is an advanced screening test, which is highly accurate. Test results reporting that a chromosomal dosage abnormality is **NOT DETECTED** are likely to be true negative results and can continue to be followed up as per your practice's protocols as appropriate for the pregnancy risk category. All test results where a chromosomal dosage abnormality is **DETECTED** should be followed up by an invasive diagnostic test (biopsy for CVS or amniotic fluid sample) for confirmatory diagnostic testing.



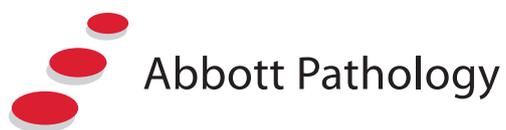
## How do I organise for my patient to be tested?

The cost of **Generation**® NIPT is \$395 (or \$450 if **Generation**® Plus NIPT is requested) and is NOT Medicare rebatable.



## More options for more patients

**Generation**® NIPT provides testing options for more of your patients, including singleton, twin, egg donor and surrogate pregnancies in the first trimester (from 10 weeks). It has been validated for use in both high-risk and low-risk patient populations. **Generation**® Plus NIPT provides additional testing options for microdeletions and trisomies 9 and 16.



Genomic Diagnostics

For more information, please visit [genomicdiagnostics.com.au](http://genomicdiagnostics.com.au) or call us on 1800 822 999

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