Generation®

a new *era* in prenatal testing

FOR MEDICAL PRACTITIONERS

Abbott Pathology

What is Generation®?

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

Generation® 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***® 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[1,2,3,4,5,6,7].

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[1,2,3,4,5,6,7].

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

- The ***Generation***® NIPT screens for the most commonly seen and tested chromosomal abnormalities including:
  - Trisomy 21 (Down syndrome)
  - Trisomy 18 (Edwards Syndrome)
  - Trisomy 13 (Patau syndrome)
  - Sex chromosomes (X and Y)
- Testing can be performed on singleton, twin, egg donor and surrogate pregnancies
- The ***Generation***® test is performed in Australia and is NATA/RCPA accredited
- The turn around time is from 5-7 days
- In our experience ***Generation***® testing has a less than 0.1% failure rate
- Genetic counselling is available for patients with "Aneuploidy detected" results from Generation® NIPT (T13,18,21 and sex chromosomes only).

Generation® Plus (for specific clinical indications as outlined below)*

- The ***Generation***® Plus NIPT screens for the most commonly tested chromosomal abnormalities from the ***Generation***® test but also more rarely occurring genetic abnormalities including:
  - 22q11 deletion (DiGeorge syndrome)
  - 15q11 deletion (Angelman/Prader-Willi)
  - 1p36 deletion syndrome
  - 4p deletion (Wolf-Hirschhorn syndrome)
  - 5p (Cri-du-chat)
- Testing can be performed on singleton, egg donor and surrogate pregnancies
- The ***Generation***® Plus test is performed in an accredited laboratory in California
- The turn around time is 9-14 days
- Genetic counselling is available for patients with "Aneuploidy detected" results for T13,18,21 and sex chromosomes only (not for microdeletion results).

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 also not tested for by NIPT.

** **Generation**® Plus includes testing for 5 microdeletion syndromes in addition to aneuploidy testing for chromosomes 13, 18, 21, X and Y. This test option should be considered when there are specific indications indicating an increased risk of one of these microdeletion syndromes. Typical clinical indications include, but are not limited to: 1. Ultrasound imaging suggestive of a specific microdeletion syndrome 2. Previous history of a pregnancy diagnosed with, or a child affected with, one of these conditions. This test is not recommended in an unselected/low risk cohort, where the **Generation**® test should be considered instead.*

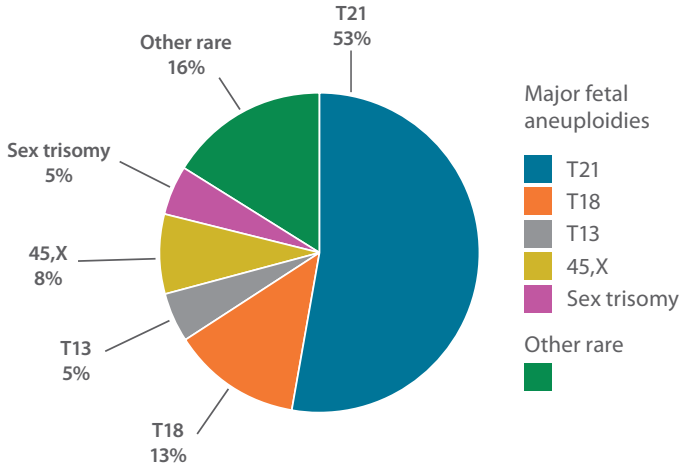
What are the performance characteristics for Generation® NIPT?

All screening tests carry a false positive rate. The ***Generation***® NIPT produces highly accurate, near diagnostic information for the most common chromosomal abnormalities [4,5,9]

	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%

* ***Generation***® Plus performance characteristics for microdeletions are not available due to limited data.

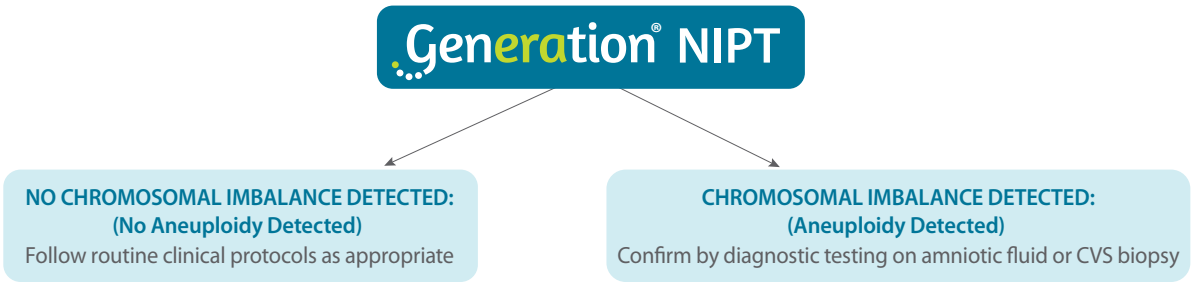
Generation® NIPT Detects 84% of Reported Chromosomal Abnormalities



Data adapted from Wellesley, D, et al., Rare chromosome abnormalities, prevalence and prenatal diagnosis rates from population-based congenital anomaly registers in Europe. *Eur J of Hum Gen* 11 January 2012.

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 (No Aneuploidy 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** (**Aneuploidy detected)** should be followed up by an invasive diagnostic test (biopsy for CVS or amniotic fluid sample) for confirmatory diagnostic testing.



We offer a genetic counselling service for patients receiving Aneuploidy Detected results. Please enquire.

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[8].

Our Experience*

<0.1%

Test Failure Rate

** Based on internal testing data for both **Generation**® NIPT and **Generation**® Plus.*

How do I organise for my patient to be tested?

This test is NOT covered by Medicare.
Full payment by credit card is required prior to blood collection.
Call 1800 822 999 (Mon-Fri, 9am-5pm AEST) to make payment and locate your nearest ***Generation***® collection centre.

1. Discuss options for prenatal testing, including ***Generation***® NIPT with your patient

2. Complete the request form with your patient (available online from www.generationNIPT.com.au)

3. Your patient contacts our Customer Care Team on 1800 822 999 to prepay and locate the most convenient collection centre

4. Please ask your patient to bring her request form to the blood collection

5. The ***Generation***® NIPT is performed

6. Results are delivered to you via your preferred method

To learn more about the Generation® prenatal test please call 1800 822 999 or visit www.generationNIPT.com.au

References

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4) Bhatt S, Parsa S, Snyder H, et al. Clinical Laboratory Experience with Noninvasive Prenatal Testing: Update on Clinically Relevant Metrics. ISPD 2014 poster.
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