Genomic Diagnostics

LEADING THE WAY TO IMPROVE HEALTH

# Generation

## A new *era* in prenatal testing

FOR MEDICAL PRACTITIONERS

Abbott Pathology | Dorevitch Pathology | Laverty Pathology | ML Pathology – Specialists in Private Pathology since the 1920s | TML Pathology – Tasmanian Medical Laboratories | Western Diagnostic Pathology

# What is Generation?

**The Generation suite of NIPT options incorporates Generation, Generation 46 and Generation Plus.**

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

These are highly sensitive, accurate, non-invasive prenatal screening tests for fetal chromosomal and subchromosomal aneuploidies. The tests use whole genome sequencing (WGS) to analyse circulating cell-free fetal DNA from a maternal blood sample from as early as 10 week's gestation.

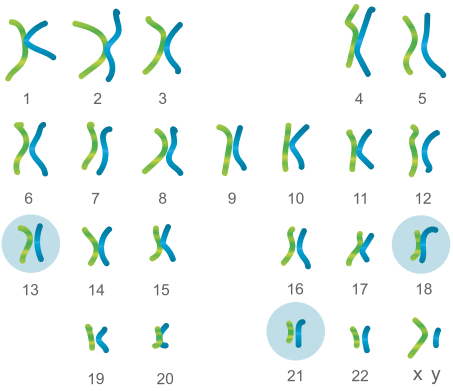
Multiple published studies of thousands of pregnant women have demonstrated the clinical utility and benefit of WGS-based NIPT, regardless of age and risk category, for both singleton and twin pregnancies.[1,2,3]

Clinical best practice guidelines from Australian and international medical societies recommend that available prenatal screening tests, including NIPT, be discussed and offered to all pregnant women.[4,5]

**Our suite of Generation NIPT tests is used to identify pregnancies at increased risk of chromosomal disorders and other pregnancy complications.**

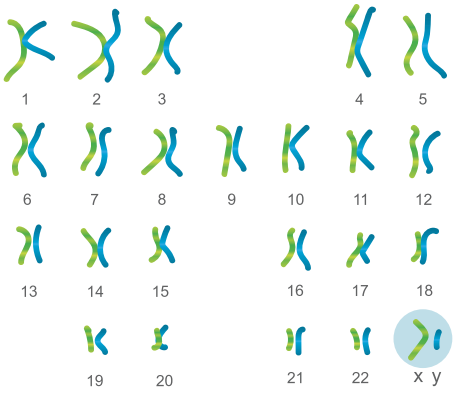
Common trisomies:

Down syndrome (T21), Edward syndrome (T18) and Patau syndrome (T13)




Sex chromosome conditions (SCA):

Including Turner syndrome (monosomy X) and Klinefelter syndrome (XXY), and XYY syndrome




Rare chromosomal and subchromosomal aneuploidies (gains or losses of whole or part of a chromosome):

Associated with significant complications such as miscarriage, IUGR, and UPD, and specific syndromes.

**Generation NIPT has the lowest reported test failure rate**

Our Experience*

<0.5%

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 stress for the patients, longer turnaround times and increased clinician visits, with high failure rates demonstrated for redraws from these patients.[6]

*Based on internal testing data for Standard Generation NIPT tested and reported on shore in Australia.

# Available Generation testing options

## Generation

***Generation*** screens for the most commonly seen and tested chromosomal abnormalities including:

- Trisomy 21 (Down syndrome), Trisomy 18 (Edwards Syndrome) and Trisomy 13 (Patau syndrome)
- Specific sex chromosome aneuploidies (monosomy X, XXX, XXY and XYY)
- Fetal sex

The ***Generation*** test is appropriate for aneuploidy screening in unselected/low risk patients.

Testing is performed in Australia and is NATA/RCPA accredited, with results available 3-5 days from the sample arriving at the laboratory*.

## Generation 46

***Generation 46*** expands on the Generation screen to include detection of aneuploidy for all 23 pairs of chromosomes:

Screening of the whole genome for chromosomal and subchromosomal aneuploidy >7Mb, including trisomies 21, 18, and 13 included in the ***Generation*** screen.

- Specific sex chromosome aneuploidies (monosomy X, XXX, XXY and XYY)
- Fetal sex

The ***Generation 46*** test is appropriate for aneuploidy screening in unselected/low risk patients. It is optimised to screen for gains and losses of at least 7Mb across the genome (excluding chromosomes X and Y). Screening for specific microdeletion syndromes is addressed by the ***Generation Plus*** test.

Testing is performed in Australia and is NATA/RCPA accredited, with results available 3-5 days from the sample arriving at the laboratory*.

## Generation Plus

***Generation Plus*** screens for the most commonly tested chromosomal abnormalities from the Generation test, as well as 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)

The ***Generation Plus*** test should be considered when there are specific clinical indications for an increased risk of one of the test microdeletion syndromes. This includes ultrasound imaging suggesting a specific microdeletion syndrome, and previous history of a pregnancy diagnosed with, or a child affected with, one of these conditions.

This test has been optimised to specifically detect the microdeletion syndromes above, but does not include genome-wide screening.

Testing is performed in an accredited laboratory in California, with results available 9-13 days from sample arriving at the laboratory*.

## All Generation Options

- Testing can be performed from 10 weeks until the end of the pregnancy
- Testing can be performed on singleton, egg donor and surrogate pregnancies
- Testing is available for twin pregnancies for ***Generation*** and ***Generation 46*** but excludes SCA screening and fetal sex determination
- Genetic counselling is available free of charge for some patients with high risk (aneuploidy detected) results. Please contact us for further information.

***Generation, Generation 46*** and ***Generation Plus*** do not test for any genetic conditions not listed above, such as 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 by NIPT.

* Samples may take several days to reach the laboratory if coming from regional Australia, or over the weekend or a public holiday.

## Accuracy of Generation NIPT

NIPT for fetal chromosomal aneuploidies has the highest detection rate and lowest false positive rate of available prenatal screening methods. Combined with the lowest reported failure rate, Generation NIPT ensures that more patients will avoid invasive diagnostic procedures.

## Performance characteristics for Generation NIPT [7]

| Chromosomal Abnormality | Sensitivity | False Positive Rate |
|---|---|---|
| Trisomy 21 | >99.9% | 0.1% |
| Trisomy 18 | >99.9% | 0.1% |
| Trisomy 13 | >99.9% | 0.1% |
| Rare Autosomal Aneuploidies | 96.4% | 0.2% |
| Subchromosomal aneuploidies >7Mb | 74.1% | 0.2% |

However, like all screening tests, not all women who receive a high-risk result will have a pregnancy with a true fetal chromosomal aneuploidy. The likelihood of a true result is different for every woman, and is determined by factors including maternal age, and personal and family medical history.

False positive results may represent chromosomal abnormalities limited to the placenta (confined placental mosaicism) or of maternal origin (maternal chromosomal aneuploidies and maternal tumours) and so diagnostic testing by amniocentesis or CVS is recommended prior to making definitive decisions regarding further pregnancy management.

## Appropriate follow up after NIPT

**Generation Low Risk Result (No aneuploidy detected)**

↓

**Monitor pregnancy as per normal protocol for risk category**

**Generation High Risk Result (Aneuploidy detected)**

↓

**Offer genetic counselling** for result discussion**

↓

**Invasive diagnostic testing (CVS or Amniocentesis) to confirm result**

**Current RANZCOG and international guidelines recommend genetic counselling for women with high risk results.

We offer a genetic counselling service for some patients with high risk (aneuploidy detected) results.
Please contact us for further information.


**References:**

1. Taneja et al. Prenat Diagn 2016 36(3);237-24 (PMID: 2671519)
2. Van der Meij et al. Am J Hum Genet 2019;105(6):1091-1101 (PMID: 31708118)
3. Gil et al. Ultrasound Obstet Gynaecol 2019;53(6):734-742. (PMID: 31165549)
4. RANZCOG guidelines for Prenatal screening and diagnostic testing for fetal chromosomal and genetic conditions, available at https://ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG- MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical-Obstetrics/Prenatal-screening_1.pdf?ext=.pdf.
5. ACOG bulletin 226, Screening for Fetal Chromosomal Abnormalities, available at https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/10/screening-for-fetal-chromosomal-abnormalities.
6. Pergament et al. Obstet Gynecol 2014; 124(201):210–218. (PMID: 250043544)
7. Illumina Veriseq NIPT Solution V2 Kit Insert available at https://support.illumina.com/content/dam/illumina-support/documents/documentation/chemistry_documentation/veriseq-nipt-v2/veriseq-nipt-solution-v2-package-insert-1000000078751-02.pdf

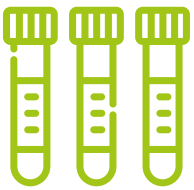
# Arranging Generation testing

## Step 1: Patient consultation

- Discuss Generation NIPT options with your patient
- Provide your patient with the request form and ensure Patient Consent section signed
- Request form available through patient software, online at genomicdiagnostic.com.au or in hard copy pads

## Step 2: Prepare for collection

- Patient is required to pay for their Generation test prior to having their blood taken
- Payment occurs online at generationnipt.com.au or over the phone on 1800 822 999
- At the time of payment, the most convenient collection to the patient is identified
- Patient notes their receipt number on the request form



## Step 3: Sample collection

- Patient attends collection centre with their signed request form
- Blood collected
- Generation testing is performed

## Step 4: Result discussion

- Results are delivered to you by preferred method
- Genetic Counselling is provided for patients with a high risk result if required
- A specific referral form is provided with all high risk results, to be completed and faxed to 03 8582 0379 should the patient wish to undertake counselling.

**This test is NOT covered by Medicare or private health funds.**

**Prepayment is required before test is collected.**

# Why choose Genomic Diagnostics?

## We're one of Australia's longest running specialist DNA testing laboratories.

We bring you depth of knowledge and experience, state of the art facilities and dedicated scientists and pathologists who care about what they do. We've been performing NIPT for over 5 years and have provided testing for many thousands of pregnancies in that time.

## Quality and Accreditation

Our laboratory has held continuous accreditation to all relevant medical testing standards for all the tests we do. We pride ourselves on providing you with quality results and expert testing advice that you can rely on.

## We're Convenient

We're part of the SDS network of pathology laboratories across Australia, which means wherever your patients are, there's a collection centre nearby.

## Dedicated, friendly and knowledgeable Customer Care team

Our customer care team specialize in taking enquiries. With extensive experience in the field, they're on hand to provide you with the right advice, or direct your enquiry, based on your requirements.

Genomic Diagnostics

LEADING THE WAY TO IMPROVE HEALTH

**For more information, contact us at info@genomicdiagnostics.com.au**

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