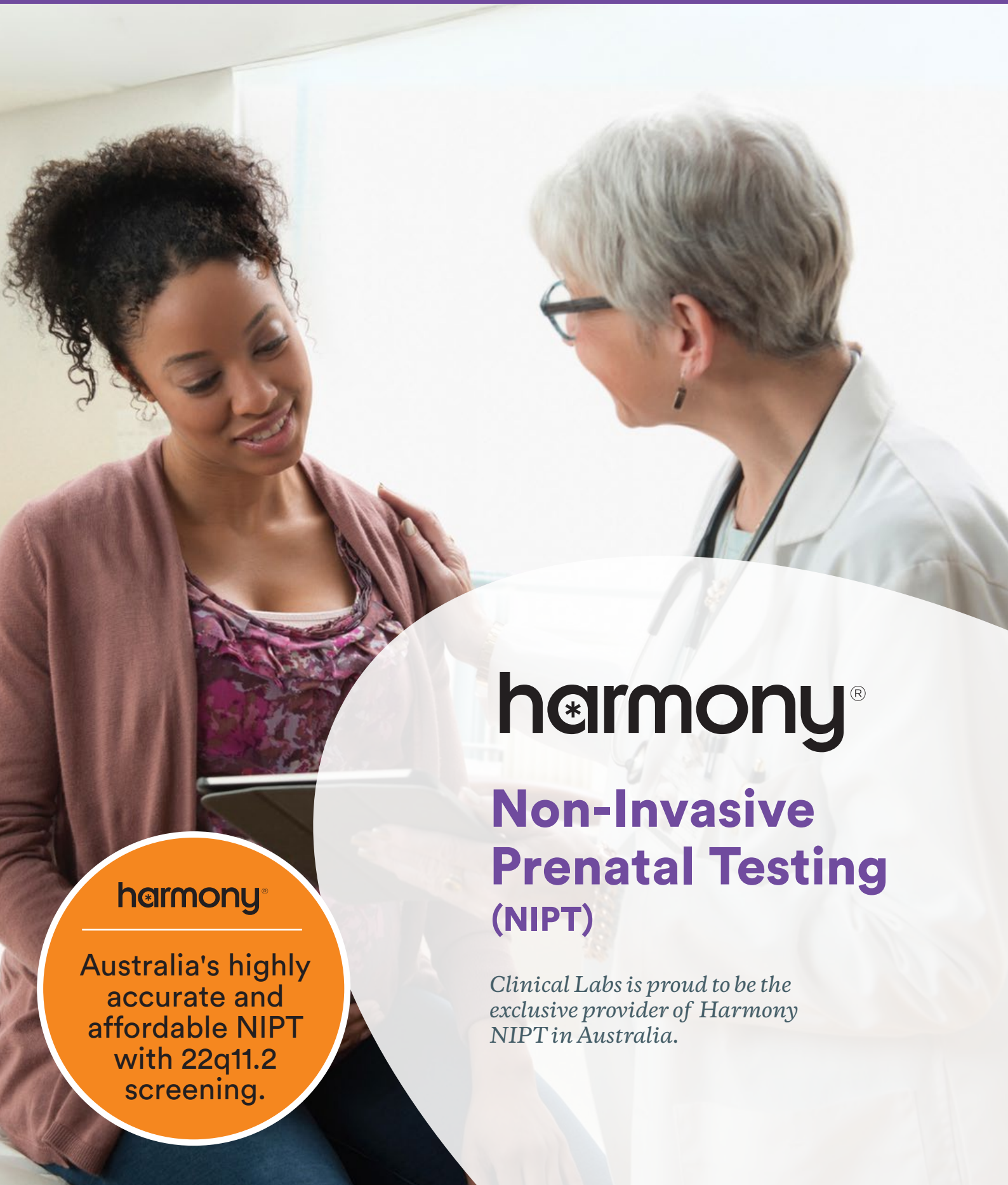
AUSTRALIAN Clinicallabs

Your experts in antenatal testing

Roche



harmony®

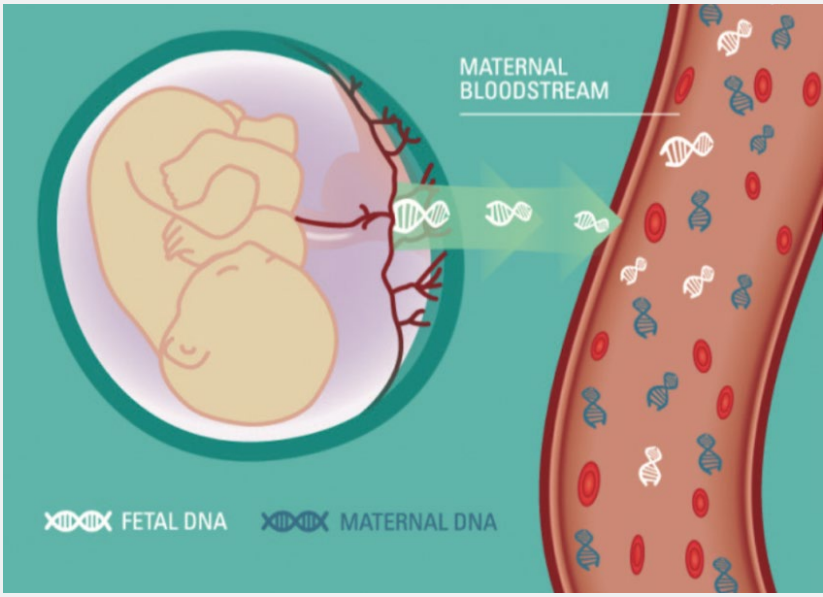
Non-Invasive Prenatal Testing (NIPT)

Clinical Labs is proud to be the exclusive provider of Harmony NIPT in Australia.

harmony®

Australia's highly accurate and affordable NIPT with 22q11.2 screening.

Harmony Non-Invasive Prenatal Testing (NIPT) is the most broadly studied non-invasive prenatal test for Down syndrome (trisomy 21), Edwards syndrome (trisomy 18), Patau syndrome (trisomy 13) and 22q11.2 deletion.[1] The test uses proprietary, targeted cell-free DNA (cfDNA) technology to analyse millions of short fragments of DNA in maternal plasma, providing both you and your patients with a greater level of assurance.[2,3,4]



Why recommend Harmony NIPT to your patients?

- Clinical Labs is the exclusive Australian provider of Harmony NIPT and is the most affordable and highly accurate choice for 22q11.2 screening in Australia. 22q11.2 deletion occurs in approximately 1 in 1,000 pregnancies[5] and is the second most common cause of developmental delay and congenital heart disease after Down syndrome[9]
- All our Harmony NIPT testing, including 22q11.2 screening, is performed in-house at our genetics laboratory, with results available within 5-10 business days
- RANZCOG recommends that NIPT should be discussed with all pregnant women.[6] Their guidelines also state that routine population-based screening for genome-wide chromosome abnormalities are not recommended due to the absence of well-performed clinical validation studies[7]
- Targeted Harmony NIPT offers exceptional specificity and sensitivity for the detection of Down syndrome: a >99% accuracy rate and a <0.1% false-positive rate[2,8]
- Harmony is available from 10+ weeks gestation, which can be earlier in the woman's pregnancy journey than conventional screening tests
- Utilising Harmony helps to reduce unnecessary invasive follow-up procedures caused by false-positive results
- Harmony can be ordered for all naturally conceived or in vitro fertilisation singleton or twin pregnancies, including those with egg donors

An NIPT recommended by clinical guidelines

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommend that NIPT should be discussed with all pregnant women.[6] The Harmony targeted cfDNA prenatal screening approach for the common trisomies provides the highest accuracy and sensitivity of this non-invasive screening test and reduces unnecessary invasive follow-up procedures caused by false-positive results.

Currently, a broader Genome Wide (GW-cfDNA) NIPT approach is not recommended by clinical guidelines and may violate World Health Organization (WHO) screening principles. Updated guidelines by the Human Genetics Society of Australasia (HGSA)/ RANZCOG 2018 state that "routine population-based screening for genome-wide chromosome abnormalities are not recommended due to the absence of well-performed clinical validation studies".[7]

For more information on the comparison between Targeted and Genome-Wide NIPT, please scan the QR code to read Associate Professor Mirette Saad's article, "*Targeted versus genome-wide non-invasive prenatal testing*."

What does Harmony NIPT screen for?

Harmony screens for the most common chromosomal conditions, including trisomies 21, 18, and 13, and optional sex chromosome aneuploidy conditions. Harmony can also evaluate fetal sex and is the most affordable and highly accurate choice for NIPT with 22q11.2 screening in Australia.

	HARMONY NIPT	OCCURENCE OF CONDITION
Down Syndrome (Trisomy 21)	✓	1 in 800 newborns
Edwards Syndrome (Trisomy 18)	✓	1 in 5,000 newborns
Patau Syndrome (Trisomy 13)	✓	1 in 16,000 newborns
Klinefelter Syndrome (47,XXY)	✓ Optional	1 in 650 newborn boys
Turner Syndrome (Monosomy X)	✓ Optional	1 in 2,500 newborn girls
Jacobs Syndrome (47,XYY)	✓ Optional	1 in 1,000 newborn boys
Triple X Syndrome (47,XXX)	✓ Optional	1 in 1,000 newborn girls
DiGeorge Syndrome (22q11.2 Deletion)	✓ Optional (at additional cost)	1 in 1,000 newborns

The quality choice for 22q11.2 screening in Australia

As part of the Harmony screening test menu, Clinical Labs offers optional 22q11.2 deletion or DiGeorge Syndrome testing. 22q11.2 deletion is the most common microdeletion syndrome, occurring in as many as 1 in 1,000 pregnancies,[5] and is the second most common cause of developmental delay and congenital heart disease after Down syndrome.[9]

Clinical Labs' Harmony NIPT with 22q11.2 is the quality choice for 22q11.2 screening in Australia. This highly accurate screening is significantly more affordable than alternative options and is performed in-house at our accredited genetics laboratory.

The features of DiGeorge syndrome vary widely. Common signs and symptoms include heart abnormalities, immune deficiency, characteristic facial features, and developmental delays, along with some laboratory biochemical abnormalities.

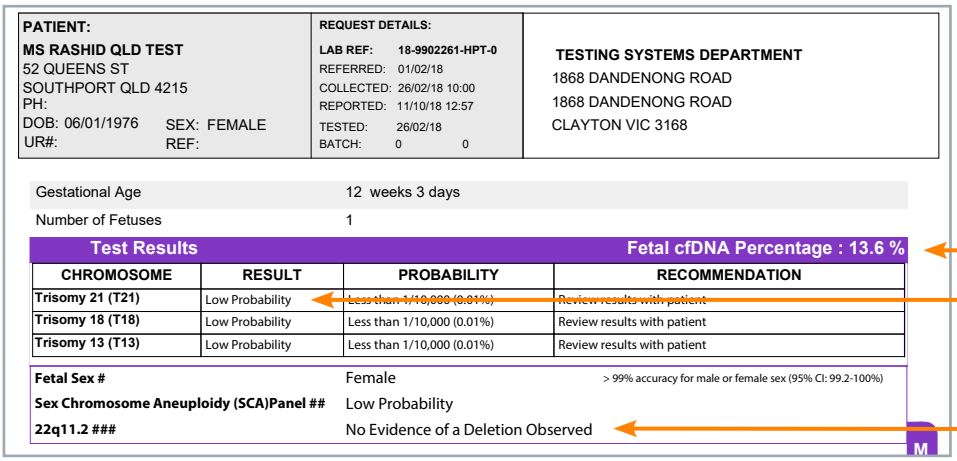
Conventional screening methods, such as first-trimester screening, do not reliably detect 22q11.2 deletion in the prenatal period.[9] Additionally, maternal age is not a risk factor for microdeletions, meaning that 22q11.2 deletion syndrome can occur in any pregnancy.[5]

The 22q11.2 deletion screening option has been validated in singleton pregnancies, including IVF self and non-self-egg donor pregnancies. However, it has not been validated in pregnancies with more than one fetus. Additionally, women with a known 22q11.2 deletion are not eligible for this test.

To access Associate Professor Mirette Saad's educational video module on *'Prenatal Screening for 22q11.2 Microdeletion'*, simply scan the QR code.

Interpreting Harmony Test Results: Sample Reports

Low probability result



PATIENT:
MS RASHID QLD TEST
52 QUEENS ST
SOUTHPORT QLD 4215
PH:
DOB: 06/01/1976 SEX: FEMALE
UR#: REF:

REQUEST DETAILS:
LAB REF: 18-9902261-HPT-0
REFERRED: 01/02/18
COLLECTED: 26/02/18 10:00
REPORTED: 11/10/18 12:57
TESTED: 26/02/18
BATCH: 0 0

TESTING SYSTEMS DEPARTMENT
1868 DANDENONG ROAD
1868 DANDENONG ROAD
CLAYTON VIC 3168

Gestational Age	12 weeks 3 days
Number of Fetuses	1

Test Results — **Fetal cfDNA Percentage : 13.6 %**

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
Trisomy 18 (T18)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
Trisomy 13 (T13)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient

Fetal Sex #	Female	> 99% accuracy for male or female sex (95% CI: 99.2-100%)
Sex Chromosome Aneuploidy (SCA)Panel ##	Low Probability	
22q11.2 ###	No Evidence of a Deletion Observed	

Fetal cfDNA Fraction %

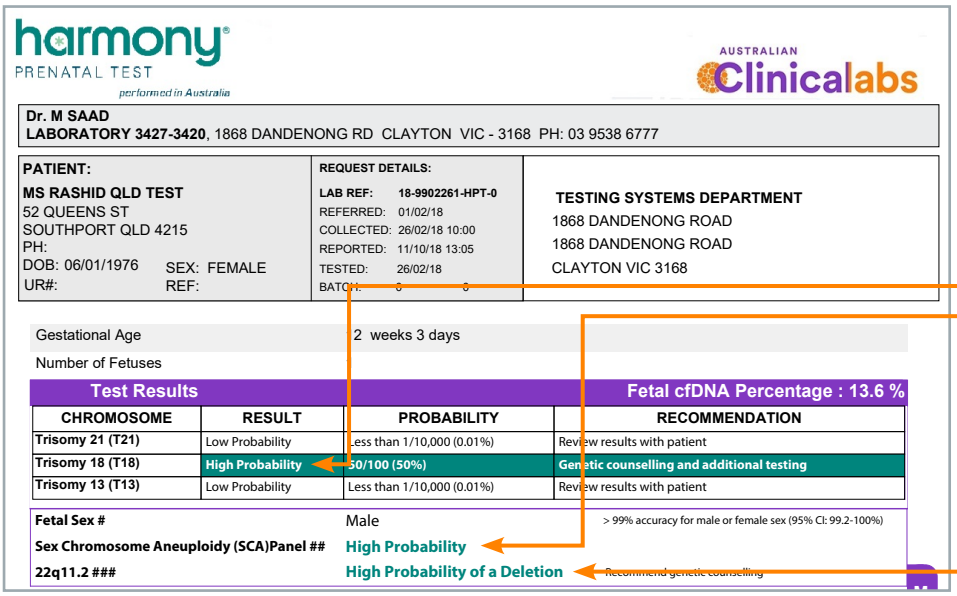
Low Probability

Highly likely that the result is correct but doesn't exclude the condition. Interpret in the clinical context.

No Evidence of Deletion Observed

It is likely that the result is correct but doesn't exclude the condition. Interpret in the clinical context.

High probability result



harmony® PRENATAL TEST performed in Australia

AUSTRALIAN Clinicalabs

Dr. M SAAD
LABORATORY 3427-3420, 1868 DANDENONG RD CLAYTON VIC - 3168 PH: 03 9538 6777

PATIENT:
MS RASHID QLD TEST
52 QUEENS ST
SOUTHPORT QLD 4215
PH:
DOB: 06/01/1976 SEX: FEMALE
UR#: REF:

REQUEST DETAILS:
LAB REF: 18-9902261-HPT-0
REFERRED: 01/02/18
COLLECTED: 26/02/18 10:00
REPORTED: 11/10/18 13:05
TESTED: 26/02/18
BATCH: 0 0

TESTING SYSTEMS DEPARTMENT
1868 DANDENONG ROAD
1868 DANDENONG ROAD
CLAYTON VIC 3168

Gestational Age	12 weeks 3 days
Number of Fetuses	1

Test Results — **Fetal cfDNA Percentage : 13.6 %**

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
Trisomy 18 (T18)	High Probability	50/100 (50%)	Genetic counselling and additional testing
Trisomy 13 (T13)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient

Fetal Sex #	Male	> 99% accuracy for male or female sex (95% CI: 99.2-100%)
Sex Chromosome Aneuploidy (SCA)Panel ##	High Probability	
22q11.2 ###	High Probability of a Deletion	Recommend genetic counselling

High Probability

It is likely but not definite that the result is correct. Confirmation is advised.

High Probability

It is likely but not definite that the result is correct. Confirmation is advised.

High Probability of a Deletion

It is likely but not definite that the result is correct. Confirmation by amniocentesis or CVS with FISH (fluorescent in-situ hybridisation) or microarray analysis should be considered.

Genetic counselling is available for high probability cases

To assist patients with high probability results, an initial telephone consultation with a certified genetic counsellor is available within 48 hours, at no additional cost. Clinical Labs will initiate the genetic counselling process for high probability cases following a doctor's referral and will provide details on how to access this service.

During the 15-20 minute phonecall, the patient can expect to discuss their Harmony prenatal test result, including a comprehensive review of how the result should be interpreted, the specified condition, a discussion surrounding additional testing options and a brief review of family history. It is also optional for the referring clinician to be involved in this call. Referring clinicians will receive a report from the genetic counsellor following the discussion. This report can further aid in the discussions between clinician and patient.

For more information about this service, including patient eligibility, please scan the QR code.

How to order Harmony

Step 1: Complete the Harmony Request Form before your patient reaches 10 weeks of pregnancy. To download the digital version or for instructions on how to access the request form through Genie, Best Practice, or MedicalDirector, please visit antenatal.clinicallabs.com.au/doctor/harmony/order.

Step 2: Please ensure that both you and the patient have signed the request form and read the detailed information on the front and back of the form.

Step 3: Once your patient reaches 10 weeks of pregnancy, they can take their signed Harmony request form to their nearest Clinical Labs collection centre (clinicallabs.com.au/location).

Step 4: Your patient will need to pay for their test at the collection centre using our online payment portal. Our collector can assist if needed.

Step 5: You will receive your patient's test results within 5-10 business days of sample receipt at our lab.

Assoc. Prof. Mirette Saad

MBBS (HONS) MD (HONS) MAACB FRCPA PHD

National Director of Molecular Genetics Australian Clinical Labs

Lab: Clayton (Vic)
Speciality: Chemical Pathology
Areas of Interest: Molecular genetics, precision medicine, cancer genetics, antenatal screening, NIPT, endocrine, fertility testing and research, medical teaching
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Associate Professor Mirette Saad is an RCPA Consultant Chemical Pathologist and the National Director of Molecular Genetics at Australian Clinical Labs. She obtained a PhD in Molecular Genetics from Melbourne University and Peter MacCallum Cancer Institute. A/P Saad chairs the RCPA Chemical Pathology Advisory Committee and is a member of the AACB and RCPA Genetic Advisory Committee.

References

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2. *Norton et al. New England J of Medicine*. 2015; 372(17): 1589-1597.
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4. Juneau *et al. Fetal Diagn Ther.* 2014. *36*(4): 282-6.
5. Grati *et al. Prenat Diagn.* 2015 Aug; *35*(8): 801-9.
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10. de Wergifosse *et al. The Journal of Maternal-Fetal & Neonatal Medicine.* 2019. DOI: 10.1080/14767058.2019.1686478.
11. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Guidelines.
12. The Royal Australian College of General Practitioners (RACGP) Guidelines.

“No call” or “Inconclusive Test” results

Between 0.5-2.9%[10] of women who undergo NIPT will not receive a result. This can be due to several factors such as insufficient fetal DNA in the sample (known as Low Fetal Fraction), high maternal BMI, early gestational age, maternal aneuploidy, chromosomal mosaicism (maternal, fetal, or placental), unknown demised co-twin pregnancy, or the mother has had a transplant or transfusions. A sample may also present an inconclusive result at 1 in 100-200 tests, if the level of "noise" (variance of genomic assays) in the sample was too great to reliably assess sex chromosomes. If the probability of trisomy 21, 18 and 13 are reported but probability of sex chromosome aneuploidy or fetal sex are inconclusive, a repeat of Harmony test is not recommended. Cumulative data showed that repeat testing is unlikely to provide a reliable result. Women with a repeated “no call” result should have a follow-up assessment, including a detailed clinical and ultrasound (if not already performed). They should be offered available options for alternative forms of screening, such as cFTS, second trimester screening, or diagnostic testing. Please note that Clinical Labs does not offer genetic counselling for "No call" or “Inconclusive Test” results. Should you wish to offer genetic counselling to your patient, this would incur an out-of-pocket fee.

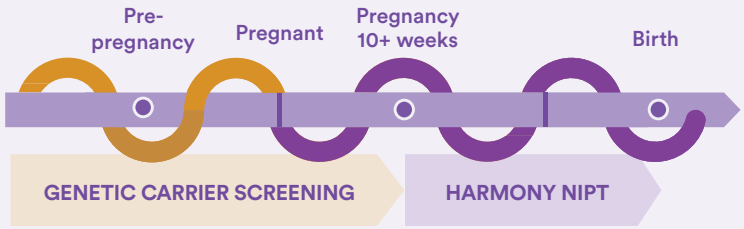
Harmony NIPT is validated for use in women ≥ 18 years and is suitable for women of any risk category. Any risk refers to the average-risk population (age < 35) and high-risk population (age > 35). Pregnancies with more than two fetuses, a history of vanishing twin, maternal organ transplant, or maternal aneuploidy are not eligible for the Harmony test. Only singleton pregnancies can undergo the sex chromosome aneuploidy and 22q11.2 deletion syndrome analysis. Harmony NIPT is a highly accurate prenatal screening test with high specificity and sensitivity. It is important to note that, while rare, false-positive and false-negative results may occur. High probability Harmony results should always be confirmed by amniocentesis/CVS before any major clinical decision is made regarding the patient’s pregnancy. The Harmony non-invasive prenatal test is based on cell-free DNA analysis and is considered a prenatal screening test. Harmony does not screen for potential chromosomal or genetic conditions other than those expressly identified in this document. The Harmony prenatal test is developed by Ariosa Diagnostics and is performed in Australia at Australian Clinical Labs.

To find out more about Harmony NIPT testing at Clinical Labs, please visit antenatal.clinicallabs.com.au/doctor/harmony.
ALWAYS FOLLOW THE DIRECTIONS FOR USE.

AUSTRALIAN Clinicallabs

Your experts in antenatal testing

Genetic Carrier Screening
Bulk-Billed & Recommended by Clinical Guidelines



As part of the wide range of antenatal tests available at Clinical Labs, we offer Bulk-Billed Genetic Carrier Screening for cystic fibrosis, spinal muscular atrophy, and fragile X syndrome, along with expanded screening options. Genetic Carrier Screening should now be a routine part of pre and early pregnancy clinical management by GPs and obstetricians, as both RANZCOG[11] and RACGP[12] guidelines recommend that genetic carrier screening be offered to every woman and couple who are planning or in the first stage of pregnancy, regardless of their risk factors.

For more information about Genetic Carrier Screening at Clinical Labs, including Medicare Eligibility Criteria, visit antenatal.clinicallabs.com.au/doctor/carrier-screening

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1300 134 111
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Roche

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