illumiscreen

A guide for healthcare providers

Expanded NIPS

Non-invasive prenatal screening

A safe, reliable and comprehensive insight about the genetic health of a pregnancy

For more information visit our website illumiscreen.co.nz

Intended use

The VeriSeq NIPT Solution v2 is an in vitro diagnostic test intended for use as a screening test for the detection of genome-wide fetal genetic anomalies from maternal peripheral whole blood specimens in pregnant women of at least 10 weeks gestation. VeriSeq NIPT Solution v2 uses whole genome sequencing to detect partial duplications and deletions for all autosomes and aneuploidy status for all chromosomes. The test offers an option to request the reporting of sex chromosome aneuploidy (SCA). This product must not be used as the sole basis for diagnosis or other pregnancy management decisions.

The Illumiscreen prenatal screen is delivered at the Labtests Laboratory, Carbine Road, Mount Wellington, Auckland, New Zealand.

An introduction to non-invasive prenatal screening (NIPS)

Non-invasive prenatal screening (NIPS) is a simple blood test that can be done from 10 weeks of pregnancy onwards to analyse the 23 chromosome pairs of a fetus' genome. The screen is a way of determining if there is an increased chance of the fetus having certain genetic conditions, due to a chromosome aneuploidy.

What is a chromosome aneuploidy?

Growth and development can be affected when there are more than 46 individual chromosomes, less than 46, or when some chromosomes have extra or missing pieces. This is called a chromosomal aneuploidy, which can lead to a chromosomal condition that have clinically relevant outcomes.

The non-invasive prenatal screening service you'll learn about in this booklet is called Illumiscreen, and is the only NIPS service in Aotearoa New Zealand where your patient's sample and information remain in the country.

How does it work?

As the fetus grows, fragments of DNA are released from the placenta into the maternal bloodstream – this is called cell-free DNA (cfDNA). These fragments are free floating and not contained within cells (unlike most DNA, which is found inside a cell's nucleus). Analysis of the cell-free DNA allows for screening of certain genetic conditions in the fetus.

Non-invasive

Illumiscreen is as safe and simple as a single blood draw

Accurate

The most accurate type of prenatal screening test for chromosome conditions, when compared to other screening tests such as maternal serum screening

Early

Can be performed as early as week 10 of gestation

Endorsed

Medical Societies endorse NIPS for all pregnant mothers regardless of age or risk[1]

Fast

Receive results in as little as 5-7 working days from the blood sample arriving at our Auckland laboratory

Conditions detected by Illumiscreen with expanded NIPS

Illumiscreen takes advantage of whole-genome sequencing (WGS) to deliver an expanded range of genetic conditions that can be screened.

This technology allows us to obtain a comprehensive view of **all 23 chromosome pairs** of the fetal genome while continuing to limit any risk to your patients.

Illumiscreen will detect the three most common pregnancy related conditions caused by a chromosomal aneuploidy, which are:

- Down syndrome (trisomy 21)
- Edward syndrome (trisomy 18)
- Patau syndrome (trisomy 13)

Trisomy means that there is an extra chromosome present on the affected chromosome pair e.g. three chromosome 21s in Downs syndrome.

Illumiscreen will now also screen for:

- **Rare autosomal aneuploidies (RAAs) –** The most common RAAs detected in NIPS involve chromosomes 7, 16, 15, and 22.
- **Partial duplications and deletions –** *Partial deletion* of a chromosome results in the loss of genetic material while duplication of chromosome results in the gain of extra copies of genetic material
- **Copy number variants (CNVs) –** This is when sections of the genome (the entire set of DNA instructions) are repeated and the number of repeats in the genome varies between individuals

Illumiscreen can also identify conditions related to **missing or extra sex chromosomes**, such as:

- Turner syndrome (only one X chromosome in a female)
- Klinefelter syndrome (an extra X chromosome in a male)
- Other possible conditions are Triple X and Jacobs syndrome

The conditions that partial duplications and deletions of chromosomes that can be screened for include, but are not limited to:

- → Cri du Chat
- → Angelman syndrome
- → DiGeorge syndrome
- → Prader-Willi syndrome
- → Wolf-Hirschhorn syndrome

These conditions can be associated with adverse clinical and pregnancy outcomes such as developmental delays, intellectual disabilities and premature labour.

Having insight into these chromosome conditions earlier may aid you and your patient in making delivery management decisions.

	Common chromosome conditions			X and Y chromosomes	Additional chromosomal conditions	
Screened condition	Trisomy 21	Trisomy 18	Trisomy 13	Sex chromosome aneuploidy	Rare autosomal aneuploidies (RAAs)	Partial deletions and duplications ≥7 Mb
Clinical association	Down syndrome	Edwards syndrome	Patau syndrome	Turner syndrome, Klinefelter syndrome, others	Early miscarriage, fetal anomalies, growth restriction, UPD, stillbirth	Fetal anomalies, developmental delay, others

Illumiscreen vs other tests

Illumiscreen uses whole-genome sequencing (WGS) technology to provide accurate non-invasive prenatal screening results with the lowest failure rate.

Illumiscreen combines low failure rates, highly accurate results, and low false-positive rates, making it one of the most reliable non-invasive prenatal screens available.

Illumiscreen uses an algorithm to increase the specific signal of aneuploid chromosomes and hence to improve the overall accuracy of classifying affected samples.

The test output further provides unambiguous results, not a risk score and is not dependent on maternal age, maternal weight, gestational age (after 10 weeks) or ethnicity.

In addition, it does not carry the risk of complications that invasive procedures do.

Highest detection rate - lowest false positive rate

As of October 2020: The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) endorse NIPS as having the highest detection rate and lowest false positive rate for the common aneuploidies regardless of maternal age or baseline risk, of all prenatal screening options.

Not a diagnostic test

It is important to note that Illumiscreen NIPS is a highly reliable non-invasive prenatal screen – it is not a diagnostic test. It will not provide a definite yes or no answer. The report will indicate if there is an increased chance the pregnancy has a chromosomal condition – see 'Reading the report in the following pages'.

To confirm an increased chance result from this screen, a diagnostic test such as amniocentesis or chorionic callus sampling (CVS) is still necessary.

As a healthcare provider, you will need to discuss these procedures and their risks with your patient.

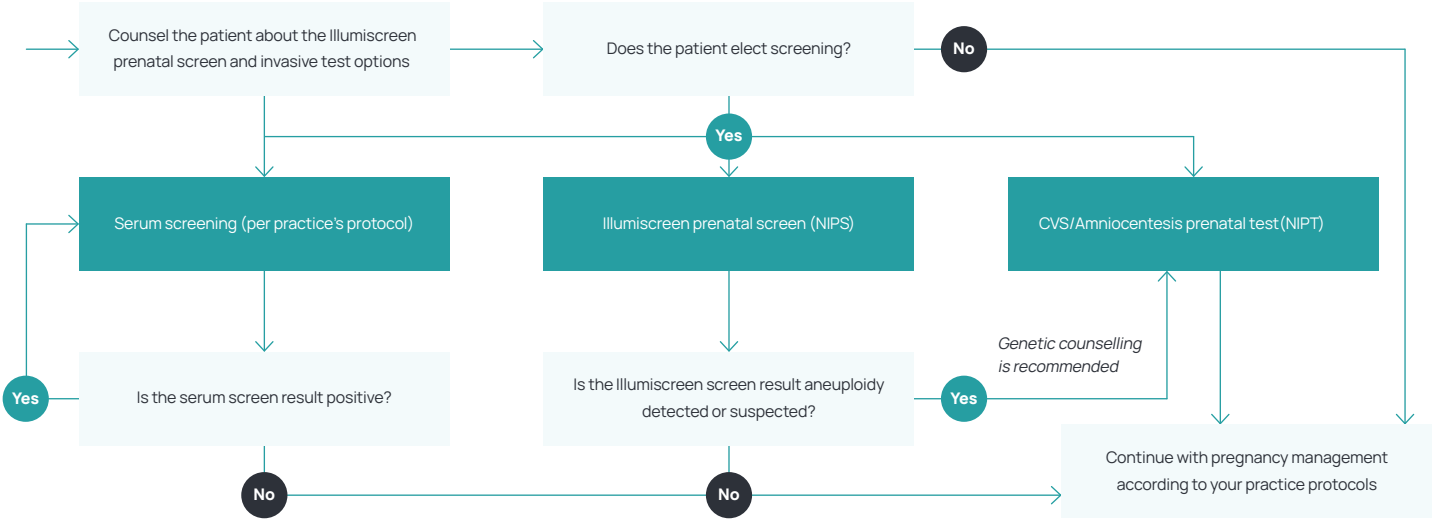
Patient management

Referring your patient

A pregnant woman can be referred for an Illumiscreen NIPS from 10 weeks gestation onwards.

This screen is often offered to pregnant women who have been identified as having a higher chance of having a baby with a chromosomal condition, however any pregnant patient can request this screen with the support of their healthcare provider, regardless of maternal age or assessed risk.

The following workflow shows where Illumiscreen sits in the patient management pathway.



Single or twin pregnancies

Illumiscreen is validated to analyse single and twin pregnancies. For twin pregnancies, only the presence of the Y chromosome can be reported when reporting the fetal sex .

Reading the report

As a healthcare provider, you will receive your patient's results which you will then need to discuss directly with them. You will also need to discuss further screening or diagnostic testing options where appropriate, or arrange for appropriate referral.

It is recommended that irreversible clinical decisions should not be made based on these screening results alone. If a definitive diagnosis is desired, chorionic villus sampling (CVS) or amniocentesis should be considered. See Patient Management for more.

The Illumiscreen NIPS result will indicate whether there is an increased chance the fetus will have a chromosomal condition through the detection of a chromosomal aneuploidy.

The report provided will include one of three possible results for chromosomes:

- **No Aneuploidy Detected** — The expected number of chromosomes were found. The result indicates a low-chance for the presence of a chromosomal condition.
- **Aneuploidy Detected** — An extra or missing copy of a chromosome has been identified. This result can indicate an increased chance for a chromosomal condition. For confirmation, a diagnostic test is advised. Genetic counselling is recommended.
- **Aneuploidy Suspected** — This is a borderline result, which occurs infrequently and suggests there might be an extra copy of a chromosome present. For confirmation, a diagnostic test is advised. Genetic counselling is recommended.

Sex chromosomes will be reported as either No Aneuploidy Detected or Aneuploidy Detected. For single pregnancies it will also show the sex of the fetus Male (XY) or Female (XX).

'Negative' results

If the Illumiscreen NIPS result shows No Aneuploidy Detected, it indicates a low-chance result, it does not completely rule out all potential issues with the fetus' chromosomes.

Although Illumiscreen is a highly reliable, non-invasive and advanced screening tool, no test can guarantee 100% that a fetus will not have any other medical or physical condition.

'Positive' results

It is important to note that Illumiscreen NIPS is a screen, not a diagnostic test. If the Illumiscreen result shows Aneuploidy Suspected or Aneuploidy Detected, it indicates a high-chance result that there might be a chromosomal condition present. The screening results need to be confirmed with diagnostic testing.

Illumiscreen NIPS results should not be used as the sole basis for pregnancy management decisions.

If your patient receives a 'positive' Illumiscreen NIPS result and you do not feel comfortable discussing the result, please refer them to a healthcare professional with appropriate expertise to discuss the reported chromosome aneuploidies, what further testing and evaluations are appropriate, and any potential clinical implications.

Testing options can include (but are not limited to):

- → Detailed ultrasound evaluation to confirm fetal viability, identify possible structural anomalies in the fetus, and/or to determine if the pregnancy is at risk for complications such as intrauterine growth restriction
- → Diagnostic testing via chorionic villus sampling or amniocentesis to determine if the positive NIPS result is indicative of a true fetal chromosomal condition, fetal mosaicism, fetal uniparental disomy, or placental mosaicism
- → Additional specialised testing e.g. karyotyping or microarray (in specific cases)

Reporting the sex of the fetus

From as early as 10 weeks, your patient can request the Illumiscreen NIPS to learn the sex of the fetus. It is important to inform your patients that all other chromosomes will also be screened, and the results will be provided in the report.

The sex of the fetus will always be included in the report whether the patient chooses this option or not, however, it is between you and your patient whether this information is disclosed to them or not.

Male sex is reported as an XY pair of sex chromosomes, and female sex is reported as an XX pair of sex chromosomes.

This result will provide the sex chromosome information for single pregnancies.

If it is a twin pregnancy, the report will indicate if there is a Y chromosome present. The presence of a Y chromosome suggests at least one twin is male, whereas the absence of a Y chromosome suggests neither twin is male.

Illumiscreen will also screen for sex aneuploidies including:

- Turner syndrome (only one X chromosome in a female)
- Klinefelter syndrome (an extra X chromosome in a male)
- Other possible conditions are Triple X and Jacobs syndrome

About our laboratory

The Illumiscreen prenatal screen is delivered at the Labtests Auckland Laboratory, Carbine Road, Mount Wellington, Auckland, New Zealand. Any Illumiscreen samples collected around New Zealand are transported to our Auckland laboratory to be processed on our specialist equipment, with our highly trained molecular scientists and technicians.

Labtests is accredited to NZS/ISO 15189 "Medical Laboratories – Particular requirements for quality and competence". The accreditation is completed annually by an external agency know as International Accreditation New Zealand (IANZ).

About Illumina

Illumina (www.illumina.com) is a leading developer, manufacturer, and marketer of life science tools and integrated systems for the analysis of genetic variation and function. We provide innovative sequencing and array-based solutions for genotyping, copy number variation analysis, methylation studies, gene expression profiling, and low-multiplex analysis of DNA, RNA, and protein.

We also provide tools and services that are fueling advances in consumer genomics and diagnostics. Our technology and products accelerate genetic analysis research and its application, paving the way for molecular medicine and ultimately transforming health care. With the acquisition of Verinata Health,

Inc., Illumina is now a leading provider of noninvasive tests for the early identification of fetal chromosomal conditions.

(1) American College of Obstetricians and Gynecologists' Committee on Practice Bulletins-Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. Am-J-Obstet Gynecol. 2020 Oct;136(4):e48-e69.

Limitations of the test

NIPS based on cfDNA analysis from maternal blood is a screening test; it is not diagnostic. False-positive and false-negative results do occur. Test results must not be used as the sole basis for diagnosis. Further confirmatory testing is necessary prior to making any irreversible pregnancy decision. A negative result does not eliminate the possibility that the pregnancy has a chromosomal or subchromosomal abnormality. This test does not screen for polyploidy (eg, triploidy), birth defects such as open neural tube defects, single-gene disorders, or other conditions, such as autism. There is a small possibility that the test results might not reflect the chromosomal status of the fetus, but may instead reflect chromosomal changes in the placenta (ie, confined placental mosaicism) or the mother that may or may not have clinical significance.

Disclaimer

The manner in which this information is used to guide patient care is the responsibility of the healthcare provider, including advising for the need for genetic counselling or additional diagnostic testing. Any diagnostic testing should be interpreted in the context of all available clinical findings.

This test was developed by, and its performance characteristics were determined by, Verinata Health, Inc., a wholly-owned subsidiary of Illumina, Inc. It has not been cleared or approved by the U. S. Food and Drug Administration. Although laboratory-developed tests to date have not been subject to U.S. FDA regulation, certification of the laboratory is required under the Clinical Laboratory Improvement Amendments (CLIA) to ensure the quality and validity of the tests. Our laboratory is CAP-accredited and certified under CLIA as qualified to perform high-complexity clinical laboratory testing.

POWERED BY illumina

Illumiscreen is powered by Illumina VeriSeqTM NIPS Solution V2

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