ILLUMI SCREEN

Next generation prenatal testing
delivered by Healthscope NZ

Medical societies agree that all pregnant women should be offered prenatal screening for fetal abnormalities and that NIPT is a major advance in screening methodologies[1–5]

THE ILLUMISCREEN PRENATAL TEST PROVIDES RELIABLE, COMPREHENSIVE ANSWERS ABOUT THE HEALTH OF A DEVELOPING FETUS

The Illumiscreen test from Illumina represents a major advance in prenatal testing, providing highly sensitive and specific answers about fetal chromosomal health—without the risks associated with invasive procedures, such as amniocentesis or chorionic villus sampling (CVS).

Performed as early as 10 weeks gestation, the Illumiscreen test demonstrates superb sensitivity and specificity for the most prevalent trisomies.

SCREENING TWIN PREGNANCIES

Screening for fetal aneuploidy in twin gestations poses unique challenges such as lower levels of DNA available for analysis from each fetus. By expanding the sensitivity and overall capability of the assay, the test can screen twin pregnancies for T21, T18, T13 and the presence of Y chromosome (optional). The test can be used in both monozygotic and dizygotic pregnancies.

COMMITTED TO RESEARCH

With its superior technology, the Illumiscreen test provides clinical evidence showing across-the-genome analysis in a real-world population. The performance of the Illumiscreen prenatal test was evaluated in a major scientific study that involved more than 60 leading US medical research and teaching institutions. The study findings were reviewed and published in the preeminent journal read by obstetricians and gynaecologists. A second study, published subsequently, presented the test's performance under regular clinical conditions and found similar results.[6] Illumina continues to expand the technology with its commitment to sponsor and support continued clinical studies to advance the effectiveness of NIPT (non-invasive prenatal testing).

Test performance in most common chromosomal aneuploides[7]

	N	Observed sensitivity	95% CI	Observed specificity	95% CI
T21 Down syndrome	577	99.14%	98.0–99.7	99.94%	99.90–99.97
T18 Edwards syndrome	175	98.31%	95.0–99.6	99.90%	99.86–99.93
T13 Patau syndrome	53	98.15%	90.0–99.9	99.95%	99.91–99.97

(For test metrics from the MELISSA validation study, please see Bianchi DW, Platt LD, Goldberg JD, et al. Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. Obstet Gynecol. 2012:119:890-901. In accordance with medical societies' requests, the observed metrics shown above are provided to reflect more recent clinical experience.)

The Illumiscreen test can also screen for sex chromosome aneuploidies in singleton pregnancies—at no extra charge

Monosomy X (Turner syndrome)	**XYY (Jacobs syndrome)**
XXX (Triple X)	**Fetal sex (XX or XY)—aids in risk stratification of X-linked disorders such as haemophilia**
XXY (Klinefelter syndrome)	

Test performance in most common sex aneuploides*[8]

	N	Sensitivity	95% CI	Specificity	95% CI	Accuracy	95% CI
MX	508	95.0% (19/20)	75.1–99.9	99.0% (483/488)	97.6–99.7	-	-
XX	508	97.6% (243/249)	94.8–99.1	99.2% (257/259)	97.2–99.9	98.4%	96.9–99.3
XY	508	99.1% (227/229)	96.9–99.9	98.9% (276/279)	96.9–99.8	99.0%	97.7–99.7

XXX, XXY, XYY: Limited data of these more rare aneuploides preclude performance calculations.

Intended use in singleton pregnancies

This screening test is intended for patients at 10 weeks or greater gestation with singleton pregnancies who meet any of the following criteria:

- Advanced maternal age (≥ 35 years at delivery)
- Positive serum screen
- Abnormal ultrasound
- History suggestive of increased risk for T21, T18, or T13, or sex chromosome aneuploidy

Intended use in twin pregnancies

This screening test is intended for patients at 10 weeks or greater gestation with twin pregnancies who meet any of the following criteria:

- Advanced maternal age (≥32 years at delivery)
- Positive serum screen
- Abnormal ultrasound
- History suggestive of increased risk for T21, T18, or T13

*Sex chromosome mosaicism cannot be distinguished by this method (the occurrence of which is < 0.3%). Patients with such mosaicism will have a sex chromosome result reported and will fall into one of the six categories (Monosomy X, XXX, XXY, XYY, XX, XY).

The Illumiscreen advantage—A more stringent and optimised approach to genetic sequencing

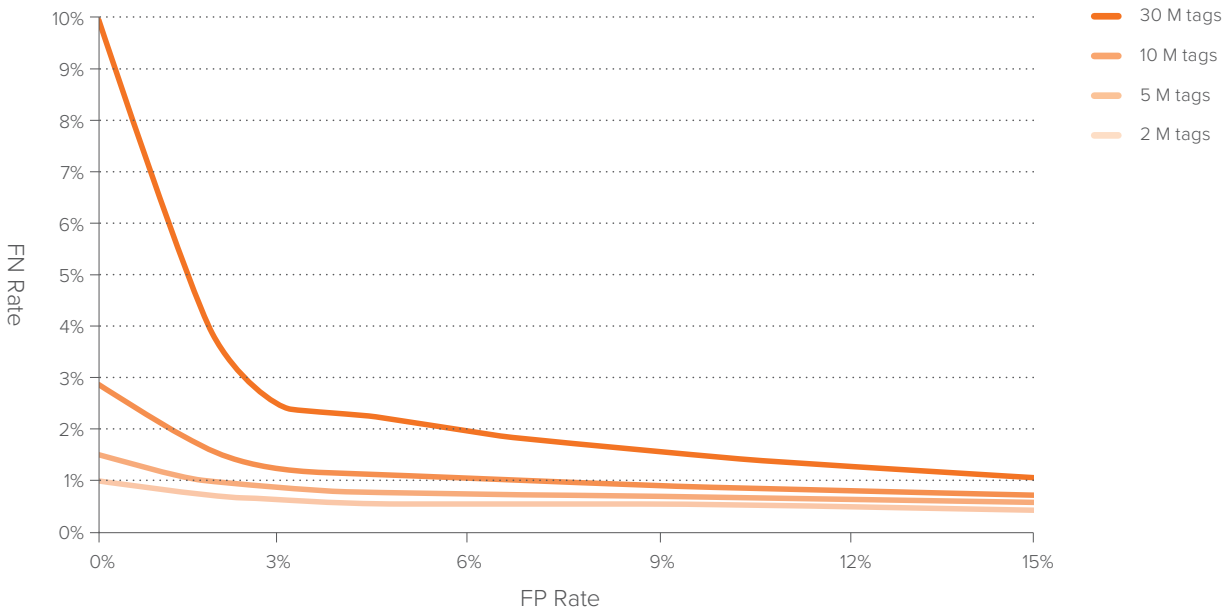
The Illumiscreen prenatal test leverages the power of massively parallel sequencing (MPS) across the whole genome. The industry's deepest sequencing approach combined with a highly optimised algorithm provides a clearer, more reliable answer than other methods.

In this graph, shallower sequencing necessitates using fetal fraction (ff) estimates as compensation for weaker sequencing power. Without ff estimates, the incidence of false negatives would be clinically unacceptable and result in higher numbers of sample rejections and delayed result time.

Other targeted noninvasive prenatal tests

Illumiscreen prenatal test: whole-genome sequencing

The science of deeper sequencing



UTILISING THE POWER OF DEEPER SEQUENCING, THE ILLUMISCREEN TEST GIVES REASSURANCE BY:

- Eliminating unnecessary sample rejections
- Reducing the need for redraws
- Obviating requests for paternal samples
- Providing fast report time for results 5-7 business days after sample receipt

THE PROOF IS IN THE DATA

Our excellent NPV and PPV results are achieved without relying on variable ff estimates or other correction factors.[7]

The Illumiscreen test with our enhanced SAFeR™ algorithm increases the specific signal of aneuploid chromosomes and hence improves the overall accuracy of classifying affected samples. The test output provides unambiguous results, not a risk score, and it is not dependent on maternal age, maternal weight, gestational age (after 10 weeks) or ethnicity.

	Positive predictive value	Negative predictive value
T21	0.970	0.999

ILLUMISCREEN TEST WITH SAFeR	OTHER TARGETED SEQUENCING TESTS
Definitive cut-off values provide clear screening results	Provides ambiguous risk scores similar to serum screens
Lowest test failure rate (0.1%)[6]	High failure rates (5%–10% or greater)
Not constrained by BMI, ethnicity, or paternal sample	May rely on BMI, ethnicity, or paternal sample to improve accuracy
Accepts egg donors	May exclude egg donors

SHEDDING NEEDED LIGHT ON FETAL CHROMOSOMAL HEALTH—SIMPLY, SAFELY, SOONER.

An easy, noninvasive blood test delivering the answers you seek in just days

The Illumiscreen prenatal test is easy to order and needs only 1 tube of blood (just a 7mL sample). Our reports are available to referrer in 5-7 business days after sample receipt.

THE ILLUMISCREEN TEST REPORT IS WELL ORGANISED AND EASY TO READ

Basic reports contain results for chromosomes 21, 18 and 13. Test reports include one of three possible results for chromosomes 21, 18, and 13: *No Aneuploidy Detected*, *Aneuploidy Detected*, or *Aneuploidy Suspected (Borderline Value)*.

For singleton pregnancies, sex chromosome results are reported in cases where requested. If there are no sex chromosome aneuploidies, then the report will indicate XX or XY status. (It is for the provider and patient to decide if the fetal sex information is to be revealed to the patient.)

It is recommended that no irreversible clinical decisions be made based on these screening results alone. If a definitive diagnosis is desired, chorionic villus sampling or anmiocentesis should be undertaken.

The Illumiscreen test has an option to screen for additional chromosomal disorders such as DiGeorge or Prader-Willi syndromes. Microdetections are available by special request and may incur additional costs.

KNOW WHAT AN ILLUMISCREEN TEST CASE LOOKS LIKE

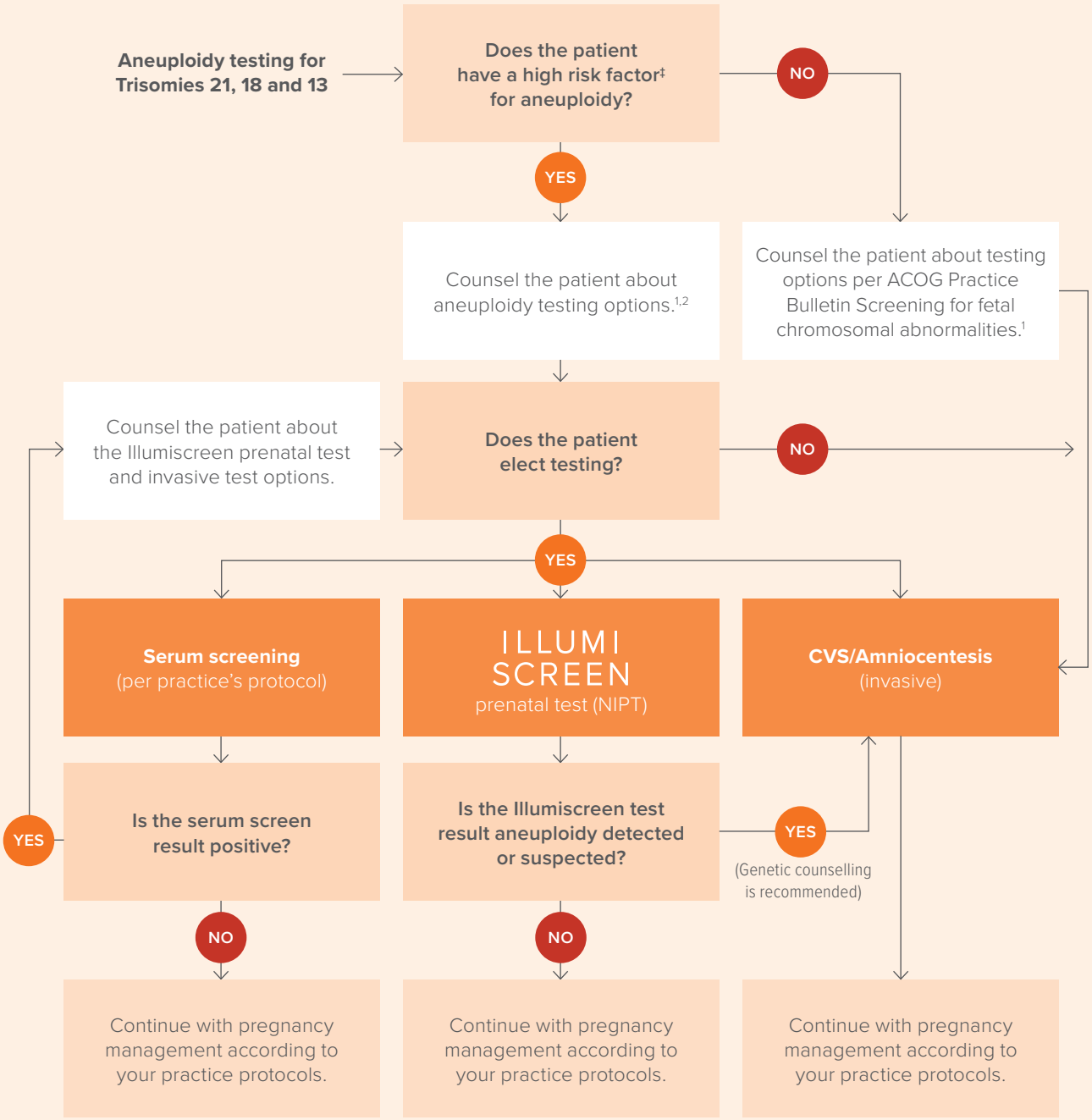
High-risk patient considering an invasive procedure.

38-year-old woman with history of infertility who conceived via *in vitro* fertilisation (IVF)

Genetic counselling to discuss testing options	– Serum screening – Invasive test —fearful of procedural loss – Illumiscreen prenatal test – Ultrasound
Patient elects the Illumiscreen prenatal test	– Chromosome 21—No Aneuploidy Detected – Chromosome 18—No Aneuploidy Detected – Chromosome 13—No Aneuploidy Detected – Normal ultrasound

Patient is comfortable declining invasive testing as she has confidence in the high sensitivity of Illumiscreen prenatal test and normal ultrasound result. Procedural risks avoided.

INCORPORATING THE ILLUMISCREEN PRENATAL TEST INTO PRACTICE



‡This workflow was developed in adherence to the current ACOG/SMFM Committee Opinion No. 545, December 2012.
Patient can choose/decline options based on clinical discussion with her provider.

Get started with the Illumiscreen prenatal test today — illumiscreen.co.nz

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 abnormalities.

Disclaimer

The manner in which this information is used to guide patient care is the responsibility of the health care 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.

Limitations of test

The Illumiscreen prenatal test is a highly accurate advanced screening test that is non-invasive. This test is designed to screen for chromosome aneuploidies and is validated for chromosomes 21, 18, and 13, X and Y. The test is validated for singleton and twin pregnancies with gestational age of at least 10 weeks. Genetic counselling before and after testing is recommended. These results do not eliminate the possibility that this pregnancy may be associated with other chromosomal abnormalities, birth defects, or other complications. A negative test result does not preclude the presence of trisomy 21, trisomy 18, or trisomy 13, monosomy X, XXX, XXY, and XYY. When an aneuploidy detected result is reported in a twin pregnancy, the status of each individual fetus cannot be determined. The presence or absence of Y chromosome material can be reported in a twin pregnancy; however, the occurrence of sex chromosome aneuploidies such as MX, XXX, XXY, and XYY, cannot be evaluated in twin pregnancies. There is a small possibility that the test results might not reflect the chromosomes of the fetus, but may reflect the chromosomal changes of the placenta (confined placental mosaicism), or of the mother (chromosomal mosaicism). Results of “Aneuploidy Detected” or “Aneuploidy Suspected” are considered positive. Illumina recommends that no irreversible clinical decisions should be made based on these screening results alone. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis would be necessary.

References

1. ACOG Committee on Practice Bulletins. ACOG Practice Bulletin No. 77: screening for fetal chromosomal abnormalities. *Obstet Gynecol.* 2007:109:217–227.
2. American College of Obstetricians and Gynaecologists Committee on Genetics. Committee Opinion No. 545: noninvasive prenatal testing for fetal aneuploidy. *Obstet Gynecol.* 2012:120:1532–1534.
3. Gregg AR, Gross SJ, Best RG, et al. ACMG statement on noninvasive prenatal screening for fetal aneuploidy. *Genet Med.* 2013:15:395–398.
4. Benn P, Borell A, Chiu R, et al. Position Statement from the Aneuploidy Screening Committee on Behalf of the Board of the International Society for Prenatal Diagnosis. *Prenat Diagn.* 2013;33:622–629.
5. Devers PL, Cronister A, Ormond KE, et al. Noninvasive prenatal testing/noninvasive prenatal diagnosis: the position of the National Society of Genetic Counselors. *J Genet Couns.* 2013:22:291–295.
6. Futch T, Spinosa J, Bhatt S, et al. Initial clinical laboratory experience in noninvasive prenatal testing for fetal aneuploidy from maternal plasma DNA samples. *Prenat Diagn.* 2013:33:569–574.
7. Bhatt S, Parsa S, Snyder H, et al. Clinical Laboratory Experience with Noninvasive Prenatal Testing: Update on Clinically Relevant Metrics. ISPD 2014 poster.
8. Verinata Health, Inc. (2012) Analytical Validation of the verifi Prenatal Test: Enhanced Test Performance For Detecting Trisomies 21, 18, and 13 and the Option for Classification of Sex Chromosome Status. Redwood City, CA.
9. Data on file: Internal data from lab metric updates.

Additional studies

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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.

Sehnert AJ, Rhees B, Comstock D, et al. Optimal detection of fetal chromosomal abnormalities by massively parallel DNA sequencing of cell-free fetal DNA from maternal blood. *Clin Chem.* 2011;57:1042–1049.

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