your questions – answered

the reassurance of knowing

verifi®
prenatal test

your questions – answered

illuminå®
The verifi® Prenatal Test provides reliable, comprehensive answers about the health of a developing fetus.

The verifi 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 verifi Test demonstrates superb sensitivity and specificity for the most prevalent trisomies.

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

Test performance in most common chromosomal aneuploides6

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Observed sensitivity</th>
<th>95% CI</th>
<th>Observed specificity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>T21</td>
<td>577</td>
<td>99.14%</td>
<td>98.0–99.7</td>
<td>99.94%</td>
<td>99.90–99.97</td>
</tr>
<tr>
<td>T18</td>
<td>175</td>
<td>98.31%</td>
<td>95.0–99.6</td>
<td>99.90%</td>
<td>99.86–99.93</td>
</tr>
<tr>
<td>T13</td>
<td>53</td>
<td>98.15%</td>
<td>90.0–99.9</td>
<td>99.95%</td>
<td>99.91–99.97</td>
</tr>
</tbody>
</table>

(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.)

*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, XY, XX, XY).
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 verifi Test provides clinical evidence showing across-the-genome analysis in a real-world population. The performance of the verifi 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 gynecologists. A second study, published subsequently, presented the test’s performance under regular clinical conditions and found similar results. 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). Illumina continues to innovate new solutions and is committed to sponsoring and supporting ongoing clinical studies to advance the effectiveness of NIPT (noninvasive prenatal testing).

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

The verifi Test can also screen for sex chromosome aneuploidies in singleton pregnancies—at no extra charge.

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

Test performance in most common sex aneuploidies*7

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

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

XXX, XXX, XXY, XYY: Limited data of these more rare aneuploidies preclude performance calculations.
The verifi Test advantage—A more stringent and optimized approach to genetic sequencing.

The verifi Prenatal Test leverages the power of Massively Parallel Sequencing (MPS) across the whole genome. The industry’s deepest sequencing approach combined with a highly optimized 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.

Utilizing the power of deeper sequencing, the verifi Test gives reassurance by:

- Eliminating unnecessary sample rejections
- Reducing the need for redraws
- Obviating requests for paternal samples
- Providing fast report time to partner laboratory: 3–5 business days after sample receipt.

(Time to report may vary based on the partner laboratory providing the test. Please refer to the partner laboratory’s website for more information.)
The proof is in the data.

Our excellent NPV and PPV results are achieved without relying on variable ff estimates or other correction factors.\(^6\)

<table>
<thead>
<tr>
<th></th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T21</strong></td>
<td>0.970</td>
<td>0.999</td>
</tr>
</tbody>
</table>

The verifi 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.

<table>
<thead>
<tr>
<th>verifi Test with SAFeR</th>
<th>Other targeted sequencing tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitive cut-off values provide clear screening results</td>
<td>Provides ambiguous risk scores similar to serum screens</td>
</tr>
<tr>
<td>Lowest test failure rate (0.1%)(^6)</td>
<td>High failure rates (5%–10% or greater)</td>
</tr>
<tr>
<td>Not constrained by BMI, ethnicity, or paternal sample</td>
<td>May rely on BMI, ethnicity, or paternal sample to improve accuracy</td>
</tr>
<tr>
<td>Accepts egg donors</td>
<td>May exclude egg donors</td>
</tr>
</tbody>
</table>
An easy, noninvasive blood test delivering the answers you seek in just days.

The verifi Prenatal Test is easy to order and needs only 1 tube of blood (just a 7mL sample). Our reports are available to the partner laboratory in 3 - 5 business days after sample receipt. (Time to report may vary based on the partner laboratory providing the test. Please refer to the partner laboratory’s website for more information.)

The verifi Test report is well organized 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 amniocentesis should be undertaken.

Know what a verifi Test case looks like.

High-risk patient considering an invasive procedure.

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

<table>
<thead>
<tr>
<th>Genetic counseling to discuss testing options</th>
<th>Serum screening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Invasive test—fearful of procedural loss</td>
</tr>
<tr>
<td></td>
<td>verifi Prenatal Test</td>
</tr>
<tr>
<td></td>
<td>Ultrasound</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient elects the verifi Prenatal Test</th>
<th>Chromosome 21—No Aneuploidy Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chromosome 18—No Aneuploidy Detected</td>
</tr>
<tr>
<td></td>
<td>Chromosome 13—No Aneuploidy Detected</td>
</tr>
<tr>
<td></td>
<td>Normal ultrasound</td>
</tr>
</tbody>
</table>

Patient is comfortable declining invasive testing as she has confidence in the high sensitivity of verifi Prenatal Test and normal ultrasound result. Procedural risks avoided.
Shedding needed light on fetal chromosomal health—simply, safely, sooner.

‡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.

Does the patient elect testing?

YES

NO

YES

Counsel the patient about aneuploidy testing options.¹ ²

Counsel the patient about testing options per ACOG Practice Bulletin Screening for fetal chromosomal abnormalities.¹

NO

YES

Counsel the patient about the verifi Prenatal Test and invasive test options.

Aneuploidy testing for Trisomies 21, 18 and 13

Incorporating the verifi Prenatal Test into practice.

Does the patient have a high risk factor for aneuploidy?

NO

YES

Counsel the patient about the verifi Prenatal Test and invasive test options.

Serum screening (per practice’s protocol)

Yes

NO

Is the serum screen result positive?

Continue with pregnancy management according to your practice’s protocols.

Continue with pregnancy management according to your practice’s protocols.

Is the verifi Test result Aneuploidy Detected or Suspected?

CVS/Amniocentesis (invasive)

YES

(Genetic counseling is recommended)

NO

Continue with pregnancy management according to your practice’s protocols.

Continue with pregnancy management according to your practice’s protocols.

Be in the know about affordable payment options.

The verifi Prenatal Test has been added to a list of in-network tests with major insurers and numerous regional plans. This means that if your patient is a member of a participating plan, the verifi Prenatal Test is a covered benefit. Members pay the lowest cost determined by their plan.

¹This 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.
Knowledgeable support.

Informed consent
Lab directors
Educational support

Illumina believes strongly in patient education and provides extensive information for informed consent. Experienced directors manage our state-of-the-art, CAP-accredited, CLIA-certified laboratory. Illumina is proud to support CME and other educational programs for health care professionals.

Get started with the verifi Prenatal Test today.
To inquire about partner laboratories in your area, contact us at 1.855.266.6563 or visit www.illumina.com/verifiproviderbrochure.

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 counseling 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 verifi 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 counseling 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, XXXYY, and XYY. If 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 MK, XXX, XXXY, and XXYY 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


Data on file: Internal data from lab metric updates.

Additional studies