# Microdeletion expansion offerings for the *verifi*® prenatal test by Pacific Rim

*verifi*® by Pacific Rim offers elective, expanded NIPT options for five of the more commonly observed and clinically relevant microdeletion syndromes and trisomies 9 and 16.

All pregnancies have a risk for being affected with a chromosome disorder, whether a microdeletion or a trisomy. Collectively, microdeletion syndromes are common, affecting approximately 1 in 1,000 pregnancies, and have clinical features that can affect growth, intellectual ability, and development. Trisomy 9 or 16 often result in a first-trimester miscarriage. These microdeletion syndromes and trisomies usually occur spontaneously without any family history. Routine prenatal serum screens cannot assess microdeletion syndromes. Additionally, microdeletion syndromes may not have abnormal ultrasound findings. Early information would aid patients and physicians greatly in pregnancy and newborn care. These expansions to the *verifi*® by Pacific Rim, the microdeletion panel and the test for trisomies 9 and 16, provide patients and physicians with additional noninvasive prenatal testing (NIPT) options based on clinical context.

Medical societies agree that all pregnant women should be offered prenatal screening and diagnosis for fetal abnormalities and that NIPT is a major advance in screening methodologies.

## Highlights

- Valuable Information
  Insight into the more commonly observed and clinically relevant microdeletion syndromes, plus trisomies 9 and 16
- Accurate Answers
  Optimized algorithm provides superior data accuracy and higher detection rates
- Responsible Testing
  Elective test available based on clinician's discretion

## Confident Results

The microdeletion and trisomies 9 and 16 testing, offered as options to the *verifi*® by Pacific Rim, use the same proven Illumina whole-genome massively parallel sequencing technology as the original test. This superior approach yields the lowest test failure rate (data on file) in the industry and confident results. Illumina technology is also the only next-generation sequencing (NGS) technology to have a peer-reviewed publication on the use of NGS to detect subchromosome microdeletions[1]. The microdeletion panel covers five of the more commonly seen and clinically relevant microdeletion regions (Table 1).

*Table 1: Performance Specifications of the verifi® by Pacific Rim. Overall Sensitivity of 91.6% and Specificity of 99.84%*

| Syndrome | 22q11.2 deletion syndrome (DiGeorge) | 1p36 deletion syndrome | Prader-Willi/ Angelman syndrome | Cri du chat syndrome | Wolf-Hirschhorn syndrome |
|---|---|---|---|---|---|
| Min. Syndrome Region Size | 2.7 Mb | 5 Mb | 5.8 Mb | 9.8 Mb | 3.6 Mb |
| **Sensitivity** | | | | | |
| No. Affected Samples Tested | 8 | 0 | 0 | 2 | 2 |
| No. Samples Detected | 7 | 0* | 0* | 2 | 2 |
| % Sensitivity [95% CI] | 87.5% [47–99] | † | † | 100% [15–100] | 100% [15–100] |
| **Specificity** | | | | | |
| No. Putative Unaffected Samples Tested | 1797 | 1797 | 1797 | 1797 | 1797 |
| No. Samples Detected | 0 | 0 | 1 | 0 | 2 |
| % Positive Call Rate | 0% [0–0.2%] | 0% [0–0.1%] | 0.05% [0.01–0.31%] | 0% [0–0.2%] | 0.11% [0.01–0.4%] |
| % Specificity [95% CI] | > 99.8% | > 99.9% | > 99.7% | > 99.8% | > 99.6% |

* Titration of fragmented genomic DNA derived from cell lines containing either a 1p36 or 15q11.2 deletion demonstrated a linear dose response and confirmed the assay's ability to measure copy number change at these loci.
† No estimates of confidence intervals or sensitivity were performed for sample sizes < 2.

## Accurate Validation

The genomic alterations associated with microdeletion syndromes are complex. The test offers an algorithm optimized for detecting these complex changes. Analytical validation is performed with several thousand samples to determine performance metrics. In addition, the test is validated using the largest number of clinical samples, providing highly accurate test sensitivity and specificity (Table 1). The validation of other NIPT assays is based on synthetic cell lines that may not mimic the complexity of the genome appropriately and cause ambiguous results.

# Taking a deeper look...

## Responsibility First

Individually, microdeletion syndromes are rare, with a low prevalence in the general population. False positive NIPT results may lead to unnecessary invasive testing. Not everyone is an appropriate candidate for additional microdeletion testing as part of their pregnancy care. Illumina is the only NIPT supplier that provides this testing as an elective option. This test should be used in the context of the patient's history, including information about family history and pregnancy information such as an abnormal ultrasound.

## Summary

Expanded NIPT options for microdeletion syndromes and trisomies 9 and 16 are now available as elective options for the proven, trusted *verifi*® prenatal test by Pacific Rim. It may provide useful information for cases with abnormal ultrasound findings or specific family histories. Superior data accuracy and higher detection rates due to comprehensive Illumina sequencing technology, combined with responsible clinical validation ensures that physicians and their patients receive results in which they can be confident.

Getting accurate results and peace of mind when your patient is at risk for microdeletion syndromes and trisomies 9 and 16…

Pacific Rim PATHOLOGY

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**www.pacificrimpathology.com**

### 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 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 Illumina. 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

This test is designed to detect subchromosomal deletions and is validated for common deletions in chromosomal regions 15q11.2, 5p15.2, 22q11.2, 1p36, and 4p16.3. The test is validated for singleton pregnancies with gestational age of at least 10 weeks as estimated by last menstrual period. These results do not eliminate the possibility that this pregnancy may be associated with other chromosomal or subchromosomal abnormalities, birth defects, and other conditions. This test is not intended to identify pregnancies at risk for open neural tube defects. A negative test result does not eliminate the possibility of Angelman syndrome, Prader-Willi syndrome, 5p-/Cri-du-Chat syndrome, 22q11.2 deletion syndrome, Williams syndrome, 1p36 deletion syndrome, or 4p-/Wolf-Hirschhorn syndrome. In addition, conditions caused by other molecular mechanisms cannot be detected with this assay. There is a small possibility that the test results might not reflect the chromosome status of the fetus, but may reflect subchromosomal changes of the placenta (confined placental mosaicism), or of the mother.

### References


1. Srinivasan A, Bianchi DW, Huang H, Sehnert AJ, Rava RP (2013) Noninvasive detection of fetal subchromosome abnormalities via deep sequencing of maternal plasma. Am J Hum Genet. 92(2): 167–176.


THIS TEST WAS DEVELOPED BY, AND ITS PERFORMANCE CHARACTERISTICS DETERMINED BY YYY IT IS NOT CLEARED OR APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION

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