Roche

harmony
PRENATAL TEST

HARMONY PRENATAL TEST is a cell-free DNA screening test for the assessment of fetal trisomies 21, 18, and 13.

The Harmony Prenatal Test was developed, and its performance characteristics determined by Ariosa Diagnostics, a CLIA and CAP accredited clinical laboratory in San Jose, CA USA. This testing service has not been cleared or approved by the US FDA.

CLIA

Exceptional Performance

AS EARLY AS 10 WEEKS, the Harmony Prenatal Test is a blood screening test for the assessment of fetal trisomy 21, 18, and 13.

Harmony is Validated for Pregnant Women of Any Age or Risk[1] and Trusted by Clinicians Worldwide

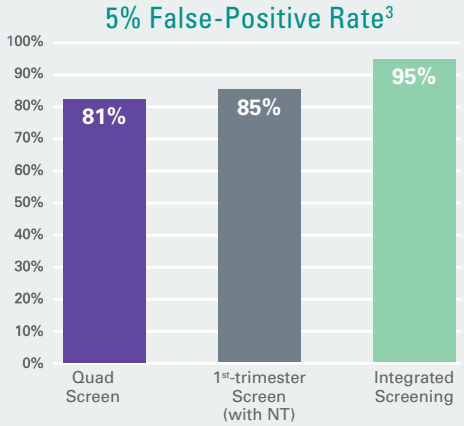
- Studied extensively in blinded prospective published trials including >22,000 pregnant women.[1]
- Clinicians in more than 100 countries have trusted the Harmony test to screen more 1 million pregnancies.[2]

Combined Harmony Performance Across All Clinical Studies[1]

	DETECTION RATE	FALSE-POSITIVE RATE
TRISOMY 21	>99%	<0.1%
TRISOMY 18	97.4%	<0.1%
TRISOMY 13	93.8%	<0.1%

** Both under 35 and over 35 age groups, studies have included women ages 18-48*

Detection Rate of Conventional Trisomy 21 Tests[3]



1 in 20 women experience false-positive results with conventional trisomy 21 tests[3]

A Proprietary, Targeted Technology

Only the **HARMONY PRENATAL TEST** uses proprietary, targeted DNA-based technology: DANSR™, FORTE™[4-6]

LAB RESULTS AS SOON AS **3 DAYS**

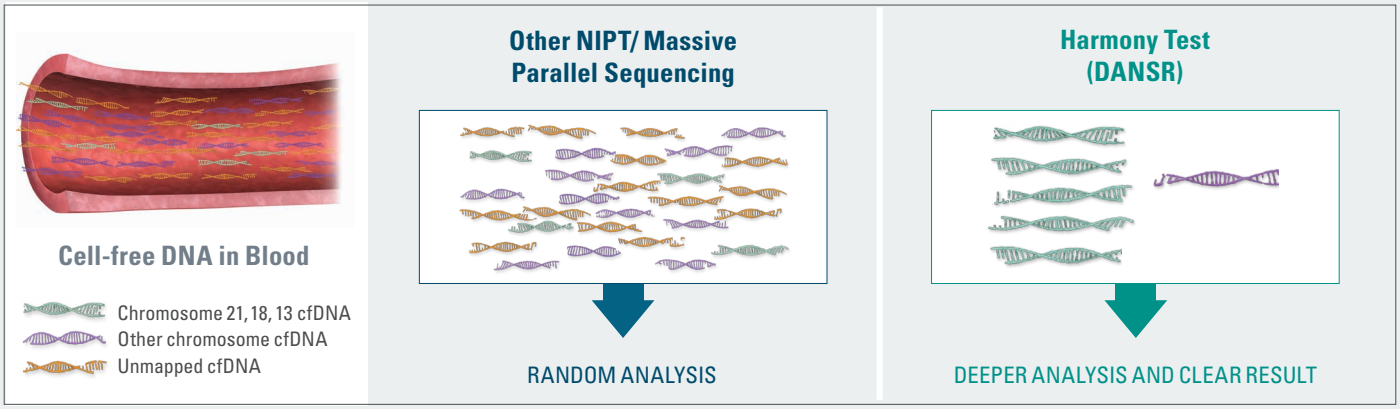
From receipt, most in 5 days

Depth of Analysis

DANSR assay targets fragments from the specific chromosomes of interest.[4]

- SNP analysis distinguishes maternal from fetal DNA and quantifies the fetal DNA [5-6]
- DNA microarray enhances speed and quality[6]

Targeted Approach Yields a Deeper Analysis versus Sequencing



Chromosomes 13, 18, and 21 together make up <10% of the genome.[7] The directed approach therefore results in a much deeper analysis as only the chromosomes of interest are targeted.[4,7, 11-12]

Accurate Measurement of Fetal Fraction

FORTE algorithm accurately distinguishes between high and low probability results even at low fetal fraction [5-6]

- Incorporates maternal risk factors and precise fetal DNA measurements
- Individual probability scores provided for each patient

Harmony Sample Test Report

Test Results — **Fetal cfDNA Percentage: 10.5%**

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	**High Probability**	**Greater than 99/100 (99%)**	**Genetic counseling and additional testing**
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

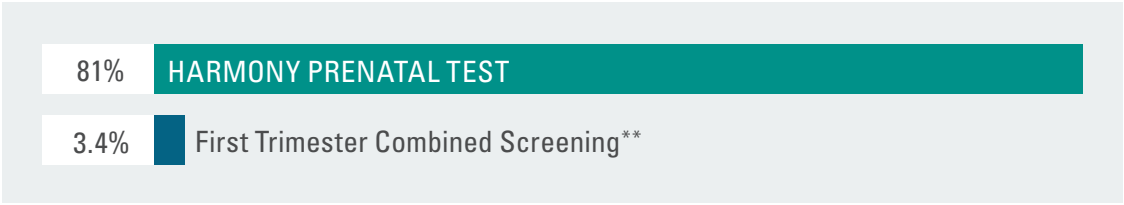
Clear Answers Early to Reduce Follow-up

The **SUPERIOR ACCURACY** and low false-positive rate of Harmony compared to traditional screening tests may minimize anxiety and invasive procedures caused by false-positive results.[8-10]

Exceptional Positive Predictive Value for the General Population

Positive Predictive Value (PPV) is the likelihood that a positive test result is a true-positive. PPV varies by population. Harmony's extremely low false-positive rate of less than 0.1% gives it a high PPV for trisomy 21.[8]

PPV in the General Population[8]



Calculated using the Harmony test *New England Journal of Medicine* study across 15,841 patients, ages 18-48. Trisomy 21 prevalence in this population was 1/417.

NIPT as a first-line primary screening test for trisomy 21.

Professional medical societies support offering aneuploidy screening, including cell-free DNA screening, to all pregnant women[3, 13-15]

ACOG/SMFM Committee Opinion Number 640: "*… any patient may choose cell-free DNA (cfDNA) analysis as a screening strategy for common aneuploidies regardless of her risk status…" (ACOG/SMFM Committee Opinion #640)* [13]

"The following protocol options are currently considered appropriate: 1. cfDNA screening as a primary test offered to all pregnant women." (ISPD Statement Aneuploidy Screening Committee, April 2015) [14]

"ACMG recommends informing all pregnant women that NIPS is the most sensitive screening option for T21,18, 13" (ACMG Statement 2016) [15]

Recommend the Harmony Test

Harmony test offers flexibility in ordering options

☑ **Harmony Prenatal Test:** Evaluates the probability for fetal trisomy 21, 18, and 13. Validated for use in twin and IVF pregnancies, including self and non-self egg donor pregnancies.[1]

Additional Test Offerings:

- ☐ Fetal sex
- ☐ Monosomy X†
- ☐ Sex chromosome aneuploidy panel†
- ☐ 22q11.2†

** *Serum PAPP-A, total or free ß-hCG & Nuchal Translucency*

† *Singletons only*

Landmark *New England Journal of Medicine* Study[8]

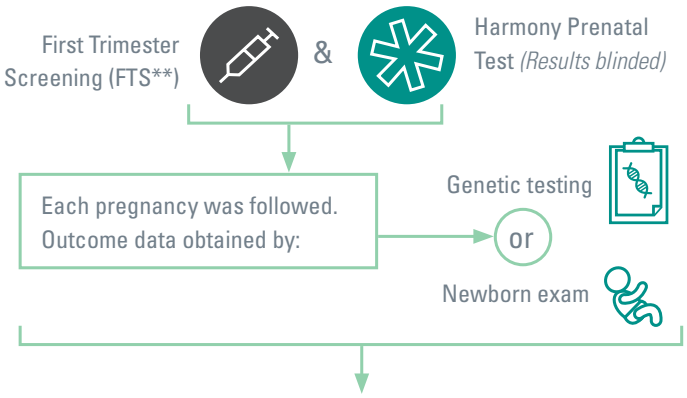
HARMONY TEST SIGNIFICANTLY OUTPERFORMS First Trimester Combined Screening (FTS**) in both trisomy 21 detection and false-positive rate in a blinded, prospective head-to-head comparison.

Study Population

Women (age 18-48, mean age 31) with singleton pregnancies between 10 to 14 weeks' gestation.

Study Design

18,955 enrolled and each woman received both:



Study Results

(n=15,841)

	FTS**	Harmony Prenatal Test	p-value
DETECTION RATE (affected pregnancies correctly identified as high risk)	**79%**	**100%**	0.008
FALSE-POSITIVE RATE (unaffected pregnancies incorrectly identified as high risk)	**5.4%**	**0.06%**	<0.001

Reducing False Positives by Over 90-fold

854 of 15,803	False positives with FTS**
9 of 15,803	**False positives with Harmony**

Exceptionally Accurate Results

- More than 1 out of 5 affected pregnancies may go undetected with FTS. Harmony is superior to FTS.

30 of 38	Sensitivity of FTS** in detecting Trisomy 21
38 of 38	**Sensitivity of Harmony in detecting Trisomy 21**

***Serum PAPP-A, total or free ß-hCG & Nuchal Translucency*

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PRENATAL TEST

Clear answers to questions that matter.

Why Choose Harmony?

- Superior accuracy for any age or risk [*7]
  - Blinded studies in over 22,000 women of any age[1]
  - Less than 0.1% false-positive rate for trisomies 21, 18, 13[1]
- Trusted by clinicians worldwide and available globally.[2]
- Performed as early as 10 weeks
- May minimize invasive procedures caused by false-positive results[9]

Three Simple Steps to Clarity

1. Draw a maternal blood sample at 10 weeks or later in pregnancy.

2. Submit sample directly to Ariosa Diagnostics or through one of our clinical laboratory partners.

3. Receive results in as little as 3 days, most in 5 days after sample receipt.

Visit us at www.harmonytest.com

For assistance email **sjc.clientservices@roche.com** or call **1-855-927-4672**
Outside the USA, call **+1 925-854-6246**

The Harmony non-invasive prenatal test is based on cell-free based on cell-free DNA analysis and is considered a prenatal screening test, not a diagnostic test. Harmony does not screen for potential chromosomal or genetic conditions other than those expressly identified in this document. Before making any treatment decisions, all women should discuss their results with their healthcare provider, who can recommend confirmatory, diagnostic testing where appropriate.

** Both under 35 and over 35 age groups, studies have included women ages 18-48*

1. Stokowski et al. Prenat Diagn. 2015 Dec;35(12):1243-6
2. Data on file
3. ACOG Committee on Practice Bulletin No.77. Obstet Gynecol. 2007 Jan;109(1):217-27.
4. Sparks et al. Prenat Diagn. 2012;32(1):3-9.
5. Sparks et al. Am J Obstet Gynecol. 2012;206(4):319.e1-9.
6. Juneau et al. Fetal Diagn Ther. 2014;36(4):282-286.
7. https://ghr.nlm.nih.gov
8. Norton et al. N Engl J Med. 2015;372(17):1589-1597.
9. Wax et al. J Clin Ultrasound. 2015 Jan;43(1):1-6
10. Lou et al. Acta Obstet Gynecol Scand. 2015 Jan;94(1):15-27.
11. Rava et al. Clin Chem. 2014 Jan;60(1):243-50.
12. Jensen et al. PLoS ONE 8(3): e57381.
13. Committee Opinion No. 640: Cell-Free DNA Screening For Fetal Aneuploidy.Obstet Gynecol. 2015 Sep;126(3):e31-7.
14. Benn et al. Prenat Diagn. 2015 Aug;35(8):725-34.
15. Gregg et al. Genet Med. 2016 Oct;18(10):1056-65.

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