

harmony®

Testing Services by Ariosa Diagnostics

Roche

PRENATAL TEST

For You

It's the assurance of reliable
and accurate results

For Her

It's confidence in results you
provide

Answers that matter

MC-US-00384

Importance of accurate measurement of fetal fraction

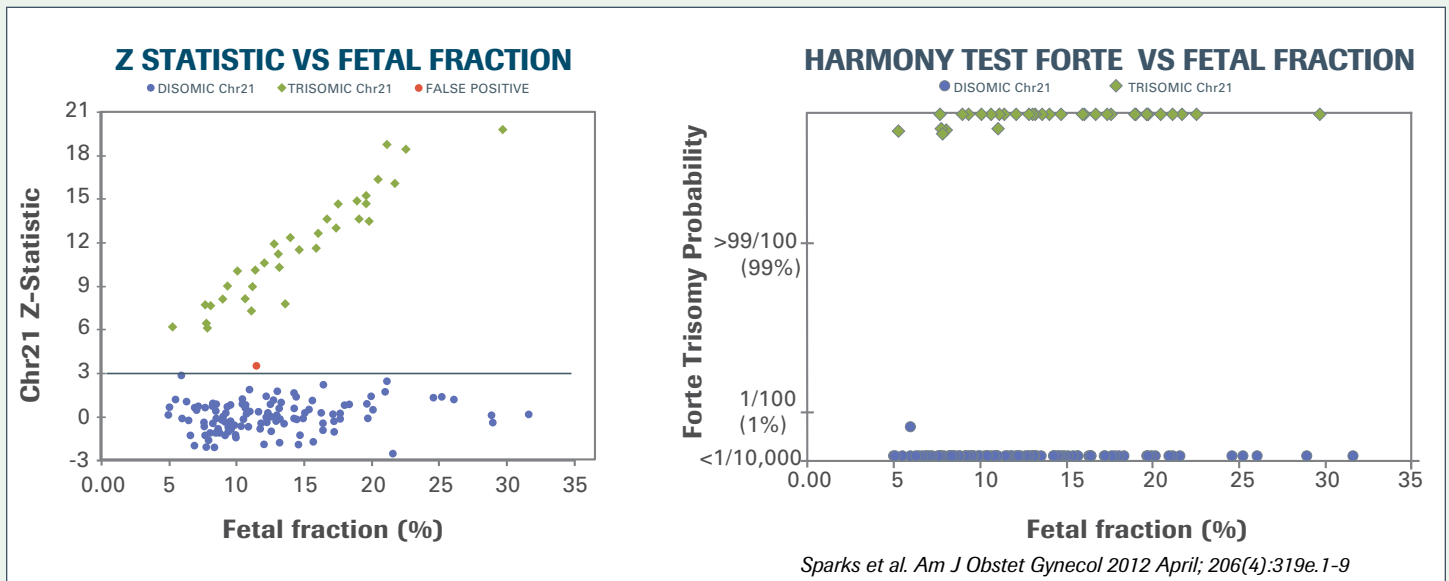
4% FETAL FRACTION, A STANDARD QUALITY METRIC FOR HARMONY FOR ACCURATE RESULTS.¹

The American College of Medical Genetics and Genomics (ACMG) position statement acknowledges that data suggest the lower limit of fetal cfDNA for a reliable result is approximately 4%.⁵

- Fetal fraction below this threshold may lead to an erroneous result of low-risk aneuploidy.^{1,6,7}
- Fetal fraction increases with gestational age and decreases with increasing maternal weight.⁸

FORTE ALGORITHM ADVANTAGES

- Clearly distinguishes high-probability and low-probability results
- Outperforms the Z-statistic approach regardless of the patient's age or risk⁴



ACCURATE MEASUREMENT OF FETAL FRACTION USING FORTE ALGORITHM

The Harmony Prenatal test measures, incorporates, and requires a minimum 4% fetal fraction as a quality control standard to ensure there is enough fetal DNA, increasing the confidence you can have in the test result.

The Harmony prenatal test measures fetal fraction using SNP technology to ensure highly accurate results, that safeguard to reduce false-negative results. The Harmony prenatal test:

- Accurately distinguishes between high- and low-probability results even at low fetal fraction⁴
- Incorporates maternal age, gestational age, fetal fraction and precise fetal DNA measurements
- Provides individual probability scores for each patient



Clinical data

NEXT STUDY RESULTS

In the landmark New England Journal of Medicine NEXT study, the Harmony Prenatal 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.⁹

General Population Study results (women 18-48)

(n=15,841)	FTS**	Harmony prenatal test
DETECTION RATE (affected pregnancies correctly identified as high risk)	79% (30 of 38)	100% (38 of 38)
FALSE-POSITIVE RATE (unaffected pregnancies incorrectly identified as high risk)	5.4% (854 of 15,803)	0.06% (9 of 15,803)

Average Risk Population Study results (women <35 years old)

(n=11,994)	Harmony Prenatal test
DETECTION RATE (affected pregnancies correctly identified as high risk)	100% (19 of 19)
FALSE-POSITIVE RATE (unaffected pregnancies incorrectly identified as high risk)	0.05% (6 of 11,994)

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

First Trimester Screening may have more than 1 out of 5 affected pregnancies go undetected.

CONSISTENTLY ACCURATE RESULTS

Combined Harmony performance across all clinical studies¹⁰

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

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 21.¹¹

81% HARMONY prenatal test (general pregnancy population)

3.4% First Trimester Combined Screening**

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

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

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

Harmony twins data

- **Validated for use in twin pregnancies**, with a higher detection rate and lower false-positive rate compared to combined (serum) screening.^{12,13}
- **Utilizing SNPs to ensure a reliable 4% fetal fraction threshold for each fetus**, to assess risk for fetal aneuploidies.^{7,14,15}
- **Minimizes possibility of false-negative results** in twin pregnancies where one twin has insufficient fetal fraction.¹⁴

22q11.2 Microdeletion

AFFECTS AS MANY AS 1 IN 1,000 PREGNANCIES

Also referred to as DiGeorge syndrome or Velo-Cardio-Facial syndrome, 22q11.2 is the second most common cause of developmental delay after Down syndrome.¹⁶⁻¹⁹

WHY CHOOSE PRENATAL SCREENING FOR 22q11.2?

- Maternal age is not a risk factor for microdeletions.¹⁸
- More than 90% of affected individuals have no family history of 22q11.2 deletion.¹⁸
- 22q11.2 deletion is not reliably detected by routine screening.¹⁹
- Early prenatal screening for 22q11.2 deletion enables informed choices and appropriate obstetrical and neonatal management.¹⁹

Services

GENETIC COUNSELING FOR YOUR PATIENT

Genetic counseling for your patient following test results is part of the Harmony Prenatal test. The counselor will review genetic test results, medical conditions, and additional genetic testing, if applicable. There is no charge to your clinic or your patient for this resource. Call 1-866-741-5331 and ask to speak with a genetic counselor.

HARMONY CARE SPECIALISTS

Prior to the blood draw, your patients can contact a Harmony Care Specialist at **1-855-927-4672** to understand their estimated out of pocket cost.

PHLEBOTOMY SERVICE

Ask your Harmony representative about the phlebotomy options in your area (if you do not have a phlebotomist on staff).

Clear answers to questions that matter

The Harmony Prenatal test assesses your patients' risk for trisomies 21, 18 and 13 as early as 10 gestational weeks. It is validated for use in pregnant women of any age* or risk category.⁹

*Both under and over 35 ages groups. Studies have included women ages 18-48.

Harmony ordering options

Trisomy 21, 18, and 13 (singleton and twins)

Fetal sex (singleton and twins)

Monosomy X (singleton only)

Sex chromosomes aneuploidy panel (single only)

22q11.2 (singleton only)

The Harmony Prenatal test has been validated for use in twins and IVF pregnancies, including self and non-self egg donor pregnancies.¹³

NIPT and 22q11.2 screening in 3 steps

- Step 1. Draw maternal blood sample at 10 weeks or later in pregnancy.*
- Step 2. Submit sample to Ariosa Diagnostics or through one of our clinical laboratory partners.
- Step 3. Receive results within 3-5 days from sample receipt at the lab.

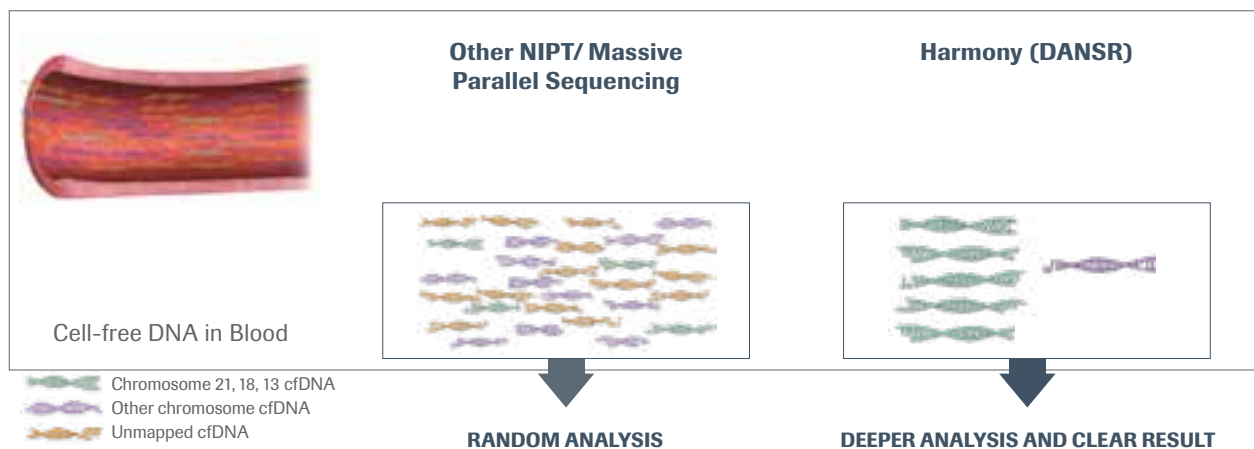
**For more information,
go to www.harmonytestusa.com
or call 1-855-927-4672.**

Why is the Harmony prenatal test right for your patients?

Harmony prenatal test relies on a proprietary, targeted DNA-based technology including both the Digital Analysis of Selected Regions (DANSR™) assay quantified on microarray and Fetal Fraction Optimized Risk of Trisomy Evaluation (FORTE™) algorithm to provide exceptionally accurate results.



Targeted approach yields a deeper analysis vs. random sequencing



Chromosomes 13, 18, and 21 together make up <10% of the genome. The directed approach therefore results in a much deeper analysis as only the chromosomes of interest are targeted.¹⁻³

DANSR TARGETED APPROACH TO DEEPER ANALYSIS VS. RANDOM SEQUENCING

Chromosomes 13, 18, and 21 together make up <10% of the genome. The directed approach results in a much deeper analysis, as only the chromosomes of interest are targeted.¹⁻³

Depth of analysis

With random sequencing, the majority of sequencing tags go to waste; they are distributed throughout all of the chromosomes. However, targeted analysis focuses all the analysis to chromosomes 21, 18 and 13. Harmony's deeper analysis is able to provide a clearer picture of the chromosomes you want to test.

SNP TECHNOLOGY

The Harmony methodology incorporates extensive quality controls:

- Single nucleotide polymorphism (SNP) analysis is used to precisely determine the fetal DNA contribution in a sample. Fetal fraction assessment is particularly important at low fetal fractions, where other methodologies have demonstrated a higher chance of discordant results.
- Harmony has a high-quality standard and requires a minimum of 4% fetal fraction. Not all cfDNA-based trisomy tests require this. Failure to do so can result in an increased chance for false-negative results.⁷

References

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- 19 McDonald-McGinn, et al. 2q11.2 deletion syndrome. 2015 Nature Reviews Disease Primers.

FOR MORE INFORMATION, GO TO WWW.HARMONYTESTUSA.COM OR CALL 1-855-927-4672.

harmonytestusa.com



The Harmony Prenatal test was developed by Ariosa Diagnostics, a CLIA-certified laboratory. As with other lab-developed tests, it has not been cleared or approved by the FDA and is not available for sales as an IVD in the U.S. Non-invasive prenatal testing (NIPT) based on cell-free DNA analysis is not diagnostic; results should be confirmed by diagnostic testing.

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Medical Approval	Ashley Allen Medical 04-Feb-2019 16:50:41 GMT+0000
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