harmony®
PRENATAL TEST
Testing service from Ariosa Diagnostics

Roche

Sample Reports Booklet

The Harmony® prenatal test is a non-invasive prenatal test (NIPT) that evaluates the probability of trisomies (trisomy 21, 18 and 13) and additional menu options, including sex chromosome aneuploidies and 22q11.2 microdeletion by analyzing cell-free DNA (cfDNA) in maternal blood. This booklet provides sample reports for the Harmony prenatal test.

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Trisomy 21, Trisomy 18, Trisomy 13 Low Probability

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www.harmonytest.com

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Ariosa Diagnostics, Inc.
5945 Optical Court
San Jose, CA 95138

Questions:

sjc.clientservices@roche.com

US: (855) 927-4672

Intl: +1 (925) 854-6246

Patient and Provider Information

PATIENT NAME: Jane Doe		ACCOUNT #: 88884
DATE OF BIRTH: (MM/DD/YYYY) 01/01/1980		CLINIC NAME: en-US Clinic Offering Test
MRN: 1234567890		REFERRING/ORDERING CLINICIAN: Ordering Provider
LABORATORY ID: AD99948736-PAT	OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:
GESTATIONAL AGE: 10 wks 5 days		OTHER CLINICIAN: Genetic Counselor MA, CGC
# OF FETUSES: 1	IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #: 123-456-7890
COLLECTION DATE (MM/DD/YYYY) : 10/23/2019	RECEIVED DATE (MM/DD/YYYY) : 10/23/2019	REPORT DATE: (MM/DD/YYYY) 10/24/2019

Test Results

Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4; Data on file.

Laboratory Director: M. Junaid Shabbeer, PhD, FACMG

TP-00115-F1 Rev 20.0
CLIA # 05D2032812

Trisomy 21 High Probability

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HIGH PROBABILITY RESULT

Patient and Provider Information

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5945 Optical Court
San Jose, CA 95138

Questions:

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US: (855) 927-4672

Intl: +1 (925) 854-6246

PATIENT NAME:	Jane Doe	ACCOUNT #:	88884
DATE OF BIRTH: (MM/DD/YYYY)	01/01/1980	CLINIC NAME:	en-US Clinic Offering Test
MRN:	1234567890	REFERRING/ORDERING CLINICIAN:	Ordering Provider
LABORATORY ID: AD99948737-PAT	OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:	
GESTATIONAL AGE:	10 wks 5 days	OTHER CLINICIAN:	Genetic Counselor MA, CGC
# OF FETUSES: 1	IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #:	123-456-7890
COLLECTION DATE (MM/DD/YYYY) : 10/23/2019	RECEIVED DATE (MM/DD/YYYY) : 10/23/2019	REPORT DATE: (MM/DD/YYYY)	10/24/2019

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

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4; Data on file.

The Harmony Prenatal Test was developed, and its performance characteristics determined, by the Ariosa Diagnostics Clinical Laboratory in San Jose, CA USA, which is certified under the Clinical Laboratory Improvement Act of 1988 (CLIA) as qualified to perform high complexity clinical testing. This testing service has not been cleared or approved by the US FDA. Harmony is a non-invasive prenatal test (NIPT) 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.

Laboratory Director: M. Junaid Shabbeer, PhD, FACMG

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CLIA # 05D2032812

Twin Pregnancy, Low Probability

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Patient and Provider Information

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Questions:

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PATIENT NAME:	Jane Doe	ACCOUNT #:	88884
DATE OF BIRTH: (MM/DD/YYYY)	04/08/1984	CLINIC NAME:	en-US Clinic Offering Test
MRN:		REFERRING/ORDERING CLINICIAN:	Ordering Provider
LABORATORY ID: AD26330167-PAT	OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:	
GESTATIONAL AGE:	21 wks 5 days	OTHER CLINICIAN:	
# OF FETUSES: 2	IVF STATUS: 25.0 yr old non-self egg donor	OTHER CLINICIAN FAX #:	408-229-7596
COLLECTION DATE (MM/DD/YYYY) : 07/08/2019	RECEIVED DATE (MM/DD/YYYY) : 07/09/2019	REPORT DATE: (MM/DD/YYYY)	07/15/2019

Test Results

Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

Fetal Sex	**Female**

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

Fetal Sex test quantifies the Y chromosome. A "female" result indicates absence of Y chromosome and a "male" result indicates presence of Y chromosome. It does not exclude sex chromosome aneuploidy. For twin pregnancies, a male result indicates one or two male fetuses.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

Fetal Sex: > 99% accuracy for male or female sex (95% CI: 99.2-100%)

Monosomy X, High Probability

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Questions:

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Patient and Provider Information

PATIENT NAME: Jane Doe	ACCOUNT #: 88884
DATE OF BIRTH: (MM/DD/YYYY) 07/02/1992	CLINIC NAME: en-US Clinic Offering Test
MRN:	REFERRING/ORDERING CLINICIAN: Ordering Provider
LABORATORY ID: AD26330165-PAT; OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:
GESTATIONAL AGE: 12 wks 4 days	OTHER CLINICIAN:
# OF FETUSES: 1; IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #: 408-229-7596
COLLECTION DATE (MM/DD/YYYY) : 07/08/2019; RECEIVED DATE (MM/DD/YYYY) : 07/09/2019	REPORT DATE: (MM/DD/YYYY) 07/15/2019

Test Results

Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

Monosomy X — **High Risk greater than 99% probability - Recommend genetic counseling**

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

Monosomy X test quantifies the X chromosome. Monosomy X is reported at a probability of 1% or greater. It does not exclude other sex chromosome aneuploidies. Monosomy X has only been validated in singleton pregnancies.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

Monosomy X: Monosomy X provides probability for non-mosaic Monosomy X. Limited numbers of Monosomy X cases have been evaluated to date.

SCAP, Low Probability

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Patient and Provider Information

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Questions:

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PATIENT NAME:	Jane Doe	ACCOUNT #:	88884
DATE OF BIRTH: (MM/DD/YYYY)	01/01/1980	CLINIC NAME:	en-US Clinic Offering Test
MRN:	1234567890	REFERRING/ORDERING CLINICIAN:	Ordering Provider
LABORATORY ID: AD99948738-PAT	OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:	
GESTATIONAL AGE:	10 wks 5 days	OTHER CLINICIAN:	Genetic Counselor MA, CGC
# OF FETUSES: 1	IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #:	123-456-7890
COLLECTION DATE (MM/DD/YYYY) : 10/23/2019	RECEIVED DATE (MM/DD/YYYY) : 10/23/2019	REPORT DATE: (MM/DD/YYYY)	10/24/2019

Test Results — Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

Sex Chromosome Aneuploidy Panel	**Low Probability**

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

Sex Chromosome Aneuploidy (SCA) Panel measures proportions of the X and Y chromosomes. Sex chromosome conditions (Monosomy X, XXY, XYY, XXX, XXYY) are reported at probabilities of 1% or greater. An XYY or XXYY result indicates two or more fetal Y chromosomes. Sex Chromosome Aneuploidy Panel has only been validated in singleton pregnancies.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

SCA Panel: SCA Panel provides probability for non-mosaic fetal sex chromosome aneuploidies. Test performance varies by condition. Limited numbers of sex chromosome aneuploidy cases have been evaluated to date.

REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4; Data on file.

Laboratory Director: M. Junaid Shabbeer, PhD, FACMG

TP-00115-F1 Rev 20.0
CLIA # 05D2032812

SCAP, Low Probability, Fetal Sex

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Patient and Provider Information

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Questions:

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US: (855) 927-4672

Intl: +1 (925) 854-6246

PATIENT NAME: Jane Doe	ACCOUNT #: 88884
DATE OF BIRTH: (MM/DD/YYYY) 01/01/1980	CLINIC NAME: en-US Clinic Offering Test
MRN: 1234567890	REFERRING/ORDERING CLINICIAN: Ordering Provider
LABORATORY ID: AD99948739-PAT OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:
GESTATIONAL AGE: 10 wks 5 days	OTHER CLINICIAN: Genetic Counselor MA, CGC
# OF FETUSES: 1 IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #: 123-456-7890
COLLECTION DATE (MM/DD/YYYY) : 10/23/2019 RECEIVED DATE (MM/DD/YYYY) : 10/23/2019	REPORT DATE: (MM/DD/YYYY) 10/24/2019

Test Results

Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

Fetal Sex	**Male**
Sex Chromosome Aneuploidy Panel	**Low Probability**

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

Fetal Sex test quantifies the Y chromosome. A "female" result indicates absence of Y chromosome and a "male" result indicates presence of Y chromosome. It does not exclude sex chromosome aneuploidy. For twin pregnancies, a male result indicates one or two male fetuses.

Sex Chromosome Aneuploidy (SCA) Panel measures proportions of the X and Y chromosomes. Sex chromosome conditions (Monosomy X, XXY, XYY, XXX, XXYY) are reported at probabilities of 1% or greater. An XYY or XXYY result indicates two or more fetal Y chromosomes. Sex Chromosome Aneuploidy Panel has only been validated in singleton pregnancies.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

Fetal Sex: > 99% accuracy for male or female sex (95% CI: 99.2-100%)

SCA Panel: SCA Panel provides probability for non-mosaic fetal sex chromosome aneuploidies. Test performance varies by condition. Limited numbers of sex chromosome aneuploidy cases have been evaluated to date.

REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4; Data on file.

The Harmony Prenatal Test was developed, and its performance characteristics determined, by the Ariosa Diagnostics Clinical Laboratory in San Jose, CA USA, which is certified under the Clinical Laboratory Improvement Act of 1988 (CLIA) as qualified to perform high complexity clinical testing. This testing service has not been cleared or approved by the US FDA. Harmony is a non-invasive prenatal test (NIPT) 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.

Laboratory Director: M. Junaid Shabbeer, PhD, FACMG

TP-00115-F1 Rev 20.0
CLIA # 05D2032812

SCAP, High Probability of Monosomy X, Fetal Sex

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Questions:

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Intl: +1 (925) 854-6246

Patient and Provider Information

PATIENT NAME:	Jane Doe	ACCOUNT #:	88884
DATE OF BIRTH: (MM/DD/YYYY)	07/31/1993	CLINIC NAME:	en-US Clinic Offering Test
MRN:		REFERRING/ORDERING CLINICIAN:	Ordering Provider
LABORATORY ID: AD26330160-PAT	OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:	
GESTATIONAL AGE:	13 wks 5 days	OTHER CLINICIAN:	
# OF FETUSES: 1	IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #:	408-229-7596
COLLECTION DATE (MM/DD/YYYY) : 07/08/2019	RECEIVED DATE (MM/DD/YYYY) : 07/09/2019	REPORT DATE: (MM/DD/YYYY)	07/15/2019

Test Results

Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

Fetal Sex	**Female**
Sex Chromosome Aneuploidy Panel	**Monosomy X greater than 99% probability - Recommend genetic counseling**

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

Fetal Sex test quantifies the Y chromosome. A "female" result indicates absence of Y chromosome and a "male" result indicates presence of Y chromosome. It does not exclude sex chromosome aneuploidy. For twin pregnancies, a male result indicates one or two male fetuses.

Sex Chromosome Aneuploidy (SCA) Panel measures proportions of the X and Y chromosomes. Sex chromosome conditions (Monosomy X, XXY, XYY, XXX, XXYY) are reported at probabilities of 1% or greater. An XYY or XXYY result indicates two or more fetal Y chromosomes. Sex Chromosome Aneuploidy Panel has only been validated in singleton pregnancies.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

Fetal Sex: > 99% accuracy for male or female sex (95% CI: 99.2-100%)

SCA Panel: SCA Panel provides probability for non-mosaic fetal sex chromosome aneuploidies. Test performance varies by condition. Limited numbers of sex chromosome aneuploidy cases have been evaluated to date.

22q11.2, No Evidence of Deletion

harmony®

www.harmonytest.com

Roche

Patient and Provider Information

Ariosa Diagnostics, Inc.
5945 Optical Court
San Jose, CA 95138

Questions:

sjc.clientservices@roche.com

US: (855) 927-4672

Intl: +1 (925) 854-6246

PATIENT NAME: Jane Doe	ACCOUNT #: 88884
DATE OF BIRTH: (MM/DD/YYYY) 01/01/1980	CLINIC NAME: en-US Clinic Offering Test
MRN: 1234567890	REFERRING/ORDERING CLINICIAN: Ordering Provider
LABORATORY ID: AD99948740-PAT / OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:
GESTATIONAL AGE: 10 wks 5 days	OTHER CLINICIAN: Genetic Counselor MA, CGC
# OF FETUSES: 1 / IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #: 123-456-7890
COLLECTION DATE (MM/DD/YYYY) : 10/23/2019 / RECEIVED DATE (MM/DD/YYYY) : 10/23/2019	REPORT DATE: (MM/DD/YYYY) 10/24/2019

Test Results

Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

22q11.2	**No evidence of a deletion observed**

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

22q11.2 test uses targeted analysis of chromosome cfDNA fragments from within a 3Mb region of 22q11.21 to determine the probability of a deletion. "High probability of a deletion" indicates that the analysis detected a decrease of cfDNA fragments consistent with a deletion in the 22q11.21 region, which may be fetal, maternal or both. "No evidence of a deletion observed" indicates the analysis does not find an increased probability for a deletion in the 22q11.21 region. Not all fetuses with 22q11.2 deletions will be classified as high probability. This test does not rule out the possibility of other clinically significant aneuploidy, single gene conditions, microdeletions or microduplications being present in the fetus. Women with a known 22q11.2 deletion are not eligible for this test. 22q11.2 test has only been validated in singleton pregnancies.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

22q11.2: Limited numbers of 22q11.2 cases have been evaluated to date.

REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4; Data on file.

The Harmony Prenatal Test was developed, and its performance characteristics determined, by the Ariosa Diagnostics Clinical Laboratory in San Jose, CA USA, which is certified under the Clinical Laboratory Improvement Act of 1988 (CLIA) as qualified to perform high complexity clinical testing. This testing service has not been cleared or approved by the US FDA. Harmony is a non-invasive prenatal test (NIPT) 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.

Laboratory Director: M. Junaid Shabbeer, PhD, FACMG

TP-00115-F1 Rev 20.0
CLIA # 05D2032812

22q11.2, High Probability

harmony®

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Patient and Provider Information

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5945 Optical Court
San Jose, CA 95138

Questions:

sjc.clientservices@roche.com

US: (855) 927-4672

Intl: +1 (925) 854-6246

PATIENT NAME:	Jane Doe	ACCOUNT #:	88884
DATE OF BIRTH: (MM/DD/YYYY)	01/01/1980	CLINIC NAME:	en-US Clinic Offering Test
MRN:	1234567890	REFERRING/ORDERING CLINICIAN:	Ordering Provider
LABORATORY ID: AD99948741-PAT	OTHER ID:	REFERRING/ORDERING CLINICIAN FAX #:	
GESTATIONAL AGE:	10 wks 5 days	OTHER CLINICIAN:	Genetic Counselor MA, CGC
# OF FETUSES: 1	IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN FAX #:	123-456-7890
COLLECTION DATE (MM/DD/YYYY) : 10/23/2019	RECEIVED DATE (MM/DD/YYYY) : 10/23/2019	REPORT DATE: (MM/DD/YYYY)	10/24/2019

Test Results

Fetal cfDNA Percentage: 10.5%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	Low Probability	Less than 1/10,000 (0.01%)	Review results with patient
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

22q11.2	High probability of a deletion - Recommend genetic counseling

TEST DESCRIPTION

The Harmony Prenatal Test® measures the relative proportion of chromosomes to aid in the assessment of fetal trisomies 21, 18, and 13. Harmony® performs a directed analysis of cell-free DNA (cfDNA) in maternal blood and incorporates the fetal fraction of cfDNA in test results. Test results also incorporate maternal age (or egg donor age) and gestational age related probability based on information provided on the test requisition form. Probability of less than 1% is defined as low probability and 1% or greater is defined as high probability. Harmony has been validated in singleton and twin pregnancies of at least 10 weeks gestational age. Harmony is not validated for use in pregnancies with more than two fetuses, demised twin, mosaicism, partial chromosome aneuploidy, translocations, maternal aneuploidy, transplant, malignancy, or in women under the age of 18. Harmony does not detect neural tube defects. Twin results reflect the probability that the pregnancy involves at least one affected fetus. Analysis of cfDNA does not always correlate with fetal genotype. Not all aneuploid fetuses will have a high probability result and some euploid fetuses will have a high probability result. The Harmony Prenatal Test is not a diagnostic test and results should be considered with other clinical criteria and communicated in a setting that includes appropriate counseling.

22q11.2 test uses targeted analysis of chromosome cfDNA fragments from within a 3Mb region of 22q11.21 to determine the probability of a deletion. "High probability of a deletion" indicates that the analysis detected a decrease of cfDNA fragments consistent with a deletion in the 22q11.21 region, which may be fetal, maternal or both. "No evidence of a deletion observed" indicates the analysis does not find an increased probability for a deletion in the 22q11.21 region. Not all fetuses with 22q11.2 deletions will be classified as high probability. This test does not rule out the possibility of other clinically significant aneuploidy, single gene conditions, microdeletions or microduplications being present in the fetus. Women with a known 22q11.2 deletion are not eligible for this test. 22q11.2 test has only been validated in singleton pregnancies.

CLINICAL DATA

	Detection Rate	False Positive Rate
T21	> 99% (95% CI: 97.9-99.8%)	< 0.1% (95% CI: 0.02-0.08%)
T18	97.4% (95% CI: 93.4-99.0%)	< 0.1% (95% CI: 0.01-0.05%)
T13	93.8% (95% CI: 79.9-98.3%)	< 0.1% (95% CI: 0.01-0.06%)

Detection and false positive (discordant result) rates based on probability cut-off of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin and egg donor pregnancies have been evaluated. The negative predictive value for trisomy 21, 18, and 13 is greater than 99%. Positive predictive value (PPV) varies by prevalence. The probability result reported is not equivalent to the PPV. For more information regarding PPV refer to: http://www.harmonytest.com/PPV

22q11.2: Limited numbers of 22q11.2 cases have been evaluated to date.

REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4; Data on file.

Laboratory Director: M. Junaid Shabbeer, PhD, FACMG

TP-00115-F1 Rev 20.0
CLIA # 05D2032812

Understanding NIPT results

What type of Harmony Prenatal test report was issued?	Why was that report issued?	What is clinically indicated next?
Low-probability result	▪ NIPT results indicate a low-probability result ▪ Most likely fetus is unaffected[1] ▪ Very low chance of false negative[1]	▪ Review results with patient[2] ▪ Continue standard prenatal care[2]
High-probability result	▪ NIPT result indicates a high-probability result for specified condition ▪ Explanations include the fetus may be affected, false positive, or maternal factors[1]	▪ Genetic counseling is recommended[2] ▪ Consideration of additional testing options[2] ▪ Call Client Services with questions: 1-855-927-4672
Specimen redraw request	▪ Reliable NIPT analysis could not be performed[3] ▪ Insufficient sample[3] ▪ Problem with sample or blood collection tubes[3] ▪ Low fetal fraction[3,4] ▪ Laboratory processing or specimen issues[3] ▪ Failure to meet thresholds for quality control[3]	▪ Take all clinical factors into account and consider obtaining another patient sample for testing[5] ▪ Review the Redraw Request report to understand the reason the result could not be obtained. ▪ Call Client Services with questions: 1-855-927-4672
Test canceled	▪ Patient doesn't meet requirements for testing (examples: gestational age less than 10 weeks, triplet gestation)[3,6] ▪ Incomplete test requisition form (TRF) after several attempts to contact office ▪ Assay failure	▪ Take all clinical and logistic factors into account and consider re-ordering the patient's Harmony test.[2] ▪ Consider alternative prenatal screening or diagnostic testing.[2] ▪ Call Client Services with questions: 1-855-927-4672
Low-probability trisomy 21, 18, and 13, but test is inconclusive for fetal sex and/or sex chromosome aneuploidy panel	▪ Technical reasons may include variance in the assay data ▪ Biological reasons may include demised co-twin, mosaicism (placental, fetal, or maternal) or copy number variant	▪ An inconclusive fetal sex and/or sex chromosome aneuploidy panel does not affect the accuracy of the trisomy screen. ▪ Repeat testing is not recommended (Repeat NIPT analysis would not be expected to yield a result) ▪ Consider alternative testing for fetal sex, such as ultrasound, and/or alternative testing for sex chromosome aneuploidies, such as diagnostic testing. ▪ Call Client Services with questions: 1-855-927-4672

COMMON REASONS FOR A SPECIMEN REDRAW REQUEST

LOW FETAL FRACTION

Approximately three percent of samples will not obtain a result, and the most common cause is due to low fetal fraction. Low FF can happen for a variety of biological reasons, including maternal weight, gestational age, and other factors that aren't well understood: ethnicity, exercise, medications, etc. Fetal cfDNA increases with gestation, decreases with increasing maternal weight, and generally provides a successful result upon second blood draw when the first attempt had insufficient fetal cfDNA.[4]

Some studies have indicated that samples with a low fetal fraction may have some higher risk of aneuploidy.[3,7]

Measuring the fetal fraction is an essential quality metric that ACOG and ACMG recommend all NIPTs should perform.

FAILURE TO MEET THRESHOLDS FOR QUALITY CONTROL

There are often technical reasons the test could not obtain a result. There may not be enough cfDNA in the sample or cfDNA of high enough quality. There may not be enough informative SNPs to accurately measure the fetal fraction in a given sample. Or there are biological factors, such as an undiagnosed vanishing twin, that can affect the results.

SPECIMEN HANDLING

The reasons for a redraw request can include having an insufficient sample size, improperly labeled tubes, and incorrect notation of twins or egg donor.

References: 1. Stokowski et al. Prenat Diagn. 2015; 35: 1243–1246. 2. ACOG Committee Position 640. Obstet Gynecol. 2015 Sep;126(3):e31-7 3. Norton et al. NEJM. 2015 Apr; 372(17):1589-97 4. Wang et al. Prenat Diagn. 2013 Jul;33(7):662-6 5. Revello et al. Ultrasound Obstet Gynecol. 2016 Jun;47(6):698-704 6. Bevilacqua et al. Ultrasound Obstet Gynecol 2015; 45: 61–66 7. Pergament et al. Obstet Gynecol 2014; 124(2 Pt 1):210-8. 8. ACMG: Gregg et al. Genet Med. 2016 Jul 18. 9. Schmid M et al. Ultrasound Obstet Gynecol. 2018 Feb 26. doi:10.1002/uog.19036

Harmony Prenatal Test Options

The Harmony Prenatal Test is validated for use in singleton, twin, and IVF pregnancies, including self and non-self egg donor pregnancies.[1]

		AVAILABLE FOR: SINGLETON	EGG DONOR & IVF	TWINS
Harmony Prenatal Test	Evaluates the probability of fetal trisomy 21, trisomy 18 and trisomy 13.	✓	✓	✓

The following test options are also available from the same blood draw:

			SINGLETON	EGG DONOR & IVF	TWINS
☐	Fetal Sex	Provides information regarding fetal sex. Assessment of fetal sex does not include assessment of sex chromosome aneuploidy. In twin pregnancies, a female result applies to both fetuses; a male result applies to one or both fetuses.	✓	✓	✓
☐	Monosomy X	Evaluates the probability of monosomy X, but no information regarding other sex chromosome aneuploidies.	✓	✓	
☐	Sex Chromosome Aneuploidy Panel	Evaluates the probability of X and Y chromosome aneuploidies, including monosomy X, XXX, XXY, XYY and XXYY.	✓	✓	
☐	22q11.2	Evaluates the probability of 22q11.2 deletion.	✓	✓	

For both Monosomy X and the Sex Chromosome Aneuploidy Panel, fetal sex will only be reported if the Fetal Sex box is checked separately. However if the result indicates a high risk for sex chromosome aneuploidy, then this risk assessment will indirectly provide information regarding fetal sex. The Harmony Prenatal test is not available for more than 2 fetuses.

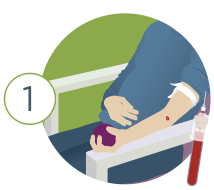
The Harmony Prenatal Test provides clear answers to questions that matter

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
- Personalized results that incorporate chromosome quantification fetal DNA fraction, gestational age, and maternal age[2-4]

Three Steps to Clarity



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

Submit sample and test requisition form per collection instructions.

Lab results in as soon as little as 3 days from receipt, most in 5 days or less.

www.harmonytest.com

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

1. Stokowski et al. Prenatal Diagnosis 2015, 35, 1–4.
2. Sparks et al. Prenat Diagn. 2012 Jan;32(1):3-9.
3. Sparks et al. Am J Obstet Gynecol. 2012 Apr;206(4):319.e1-9.
4. Juneau et al. Fetal Diagn Ther. 2014;36(4):282-6.

This testing service has not been cleared or approved by the US FDA.

Harmony is a non-invasive prenatal test (NIPT) 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.

For assistance email sjc.clientservices@roche.com or call 1-855-927-4672

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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