NHS
East Lancashire Hospitals
NHS Trust

ANTENATAL CLINIC
BURNLEY GENERAL HOSPITAL
CASTERTON AVENUE
BURNLEY
LANCASHIRE BB10 2PQ

Telephone 01282 804374
Patient Hospital No:

NHS NO

30th April 2019

Dear

We are writing to inform you that the screening test taken on DATE shows that you are in the lower chance group for having a babies with Down's Syndrome.

This is a screening test only and not a diagnosis.

The chance of Down's Syndrome is Twin One 1: number
Twin Two 1: number

This means that Twin 1 has one chance in number that the baby has the condition.
This means that Twin 2 has one chance in number that the baby has the condition.

The chance of twin 1 and twin 2 with combined Edwards' and Patau's syndrome is 1 chance in number

We would not normally offer further testing with these results, however, if you have any further queries please do not hesitate to contact us.

Please show this letter to your midwife at your next visit.

Yours sincerely

Antenatal and New Born Screening Co-ordinator

NHS
East Lancashire Hospitals
NHS Trust

ANTENATAL CLINIC
BURNLEY GENERAL HOSPITAL
CASTERTON AVENUE
BURNLEY
LANCASHIRE BB10 2PQ

Telephone 01282 804374
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30th April 2019

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This is a screening test only and not a diagnosis.

The chance of Down's Syndrome is Twin One 1: number
Twin Two 1: number

This means that Twin 1 has one chance in number that the baby has the condition.
This means that Twin 2 has one chance in number that the baby has the condition.

We would not normally offer further testing with these results, however, if you have any further queries please do not hesitate to contact us.

Please show this letter to your midwife at your next visit.

Yours sincerely

Antenatal and New Born Screening Co-ordinator

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ANTENATAL CLINIC
BURNLEY GENERAL HOSPITAL
CASTERTON AVENUE
BURNLEY
LANCASHIRE BB10 2PQ

Telephone 01282 804374
Patient Hospital No:

NHS NO.

30th April 2019

Dear

Combined screening for Edwards' and Patau's Syndromes

We are writing to inform you that the screening performed on DATE shows that you are in the lower chance group for having a baby with Edwards' and Patau's Syndromes.

This is a screening test only and not a diagnosis.

The chance of Edwards' and Patau's syndrome is 1: number this means there is one chance in number that the baby has the condition.

We would not normally offer further testing with these results, however, if you have any further queries please do not hesitate to contact us.

Please show this letter to your midwife at your next visit.

Yours sincerely

Antenatal and New Born Screening Co-ordinator

NHS
East Lancashire Hospitals
NHS Trust

ANTENATAL CLINIC
BURNLEY GENERAL HOSPITAL
CASTERTON AVENUE
BURNLEY
LANCASHIRE BB10 2PQ

Telephone 01282 804374
Patient Hospital No

NHS NO.

09

30th April 2019

Dear

Combined screening for Down's Syndrome, Edwards' and Patau's Syndromes

We are writing to inform you that the screening performed on DATE shows that you are in the lower chance group for having a baby with Down's Syndrome, Edwards' and Patau's syndromes.

This is a screening test only and not a diagnosis.

The chance of Down's Syndrome is 1:number this means that there is one chance in number that the baby has the condition.

The chance of Edwards' and Patau's syndromes is 1:number which means that there is one chance in number that the baby has the condtion.

We would not normally offer further testing with these results, however, if you have any further queries please do not hesitate to contact us.

Please show this letter to your midwife at your next visit.

Yours sincerely

Antenatal and New Born Screening Co-ordinator

Q9

East Lancashire Hospitals
NHS Trust

ANTENATAL CLINIC
BURNLEY GENERAL HOSPITAL
CASTERTON AVENUE
BURNLEY
LANCASHIRE BB10 2PQ

Telephone 01282 804374
Patient Hospital No:

NHS NO

30th April 2019

Dear

Maternal Serum Screening for Down's Syndrome

We are writing to inform you that the quadruple blood test sample taken on DATE shows that you are in the lower chance group for having a baby with Down's Syndrome.

This is a screening test only and not a diagnosis.

The chance of Down's Syndrome is 1:number this means that there is one chance in number that the baby has the condition.

We would not normally offer further testing with these results, however, if you have any further queries please do not hesitate to contact us.

Please show this letter to your midwife at your next visit.

Yours sincerely

Antenatal and New Born Screening Co-ordinator

QG

East Lancashire Hospitals NHS Trust
ANTENATAL CLINIC
BURNLEY GENERAL HOSPITAL
CASTERTON AVENUE
BURNLEY
LANCASHIRE BB10 2PQ

Telephone 01282 804374
Patient Hospital No:

NHS NO

30th April 2019

Dear

Combined screening for Down's Syndrome

We are writing to inform you that the screening performed on DATE shows that you are in the lower chance group for having a baby with Down's Syndrome.

This is a screening test only and not a diagnosis.

The chance of Down's Syndrome is 1:number this means that there is one chance in number that the baby has the condition.

We would not normally offer further testing with these results, however, if you have any further queries please do not hesitate to contact us.

Please show this letter to your midwife at your next visit.

Yours sincerely

Antenatal and New Born Screening Co-ordinator

East Lancashire Hospitals
NHS Trust
Lancashire Women & Newborn Centre
Casterton Avenue
Burnley
BB10 2PQ

Screening co-ordinator: Janyce Sutherland
Tel: 01282 803019
Email: Janyce.Sutherland@elht.nhs.uk

Hospital N
NHS No.:
Date 09/(

Non-Invasive Prenatal Testing (NIPT) Results

Patient:

Exam date:

Indication	Raised risk on combined screening
History	Risk 1:110 of trisomy 21
Pregnancy	Singleton pregnancy. Number of fetuses: 1.
Test Results	Please find enclosed the results of your recent Harmony Non-Invasive Prenatal Test (NIPT).

The results indicate that you are LOW PROBABILITY for Trisomy 21 (Down Syndrome), Trisomy 18 (Edward Syndrome) and Trisomy 13 (Patau Syndrome).

The screen for sex chromosome problems has come back as LOW PROBABILITY.

The fetal sex was determined to be MALE.

The amount of fetal cells within the blood test was deemed sufficient to analyse the sample (fetal fraction 21%).

As you recall, we discussed that the NIPT is not a diagnostic test so will not detect all cases of chromosome problems. Only invasive tests (amniocentesis) are diagnostic at this stage. If you wish to proceed with an invasive test at this stage please contact the screening team.

The test will not detect mosaicism, partial chromosome problems, translocations or maternal chromosomal problems. Harmony does not detect structural problems with your baby - these are best detected at your 20-week anomaly scan.

Follow-up — No further screening tests have been arranged at this stage.

If you wish to proceed with an invasive test (amniocentesis) please contact the screening midwives on the number above and they will arrange this for you in the Fetal Medicine Unit.

If you wish to discuss the test any further please feel free to contact my secretary on 01282-803197.

Consultant Obstetrician

EC

East Lancashire Hospitals
NHS Trust
Lancashire Women & Newborn Centre
Casterton Avenue
Burnley
BB10 2PQ

Screening co-ordinator: Janyce Sutherland
Tel: 01282 803019
Email: Janyce.Sutherland@elht.nhs.uk

Hospital No
NHS No.
Date O

Non-invasive Prenatal Testing (NIPT)

Patient:

Exam date:

Indication	Raised risk on combined screening
History	Risk 1:110 of trisomy 21
Pregnancy	Singleton pregnancy. Number of fetuses: 1.
Counselling Summary	Attended for Non-Invasive Prenatal Testing (NIPT) due to raised risk of trisomy 21 on combined screening.

Explained that this is a private test not available on NHS at present.
Harmony is the company of choice in ELHT, but other providers are available privately. Cost of the test is £350 (Harmony will invoice you for this directly).

Discussed that screening for fetal chromosomal disorders is optional. Implications for the test results discussed. The decision to proceed is based on how each individual perceives the benefits of obtaining the information about chromosomal problems when weighed against the potential emotional and physical risks of testing.

NIPT is a screening test. It cannot diagnose or eliminate the chance that a fetus has a particular chromosomal condition; rather it separates women into high and low risk categories. Testing is performed using a blood test of mother from the arm and is not associated with an increased risk of miscarriage.

We discussed that the only diagnostic test at this gestation is an amniocentesis test. This is a test where a small needle is placed through your abdomen under ultrasound guidance and a small amount of fluid surrounding the baby is taken for analysis. This will confirm if the baby is affected by a chromosomal condition. There is a small risk of 0.5-1% of

miscarriage.

Clinical features of each condition screened for in the test discussed. These included:
- Trisomy 21 (Down Syndrome)
- Trisomy 18 (Edwards Syndrome)
- Trisomy 13 (Patau Syndrome)
- Sex chromosome aneuploidies (monosomy X, XXY, XXX, XYY) . The test for this is optional. You decided that you want to proceed with this test.
- Sex of the fetus. This test is optional. You have expressed that you wish this test to be performed.

Specific testing methods discussed – there are fragments of chromosomes that circulate outside of cells within the mothers blood. These DNA fragments are referred to as 'cell-free'. Most cell free DNA fragments derive from the mothers blood cells, but some come from the placenta. Because the fetus and placenta derive from the same fertilised cell, they are usually genetically identical. The sequences of cell free DNA fragments are analysed to establish how many fragments there are and which chromosomes they have come from. The laboratory counts the number of fragments from each chromosome of interest, and determines if there are more or less than expected. If, for example, there are more than expected number of fragments from chromosome 21, this indicates an increased chance of the baby having trisomy 21.

The results will be communicated from the test laboratory to East Lancashire Hospitals and communicated to you once this has been received. A result is normally available in 3-5 working days, but can sometimes be longer than this. If you do not hear anything back after 7 working days please contact Mr Maher's secretary or the screening team.

In 3 out of 100 women a repeat test will be required (a result is achieved in approximately two thirds of these). This is because the amount of fetal blood cells in your circulation is not enough for the laboratory to test. This is called the fetal fraction. If the test requires repeating you will not be charged for this.

NIPT is not diagnostic but a screening test. This means that the test has a certain sensitivity for each condition and can sometimes be wrong..
We discussed the sensitivity for Trisomy 21 is over 99% (false positive rate <0.1%)
Trisomy 18 is 97.4% (false positive rate <0.1%)
Trisomy 13 is 93.8% (false positive rate <0.1%)
I explained that the result will give a high or low risk result. If you wish to consider invasive/diagnostic tests following the results these can be arranged in the Fetal Medicine Unit.

Following counselling today, you wished to proceed with the test and written consent was obtained for this.
Ultrasound scan confirms a viable pregnancy.
Blood samples have been taken today using an aseptic non-touch technique and sent by recorded mail to the Harmony laboratory.

Follow-up Results will normally be available in 3-5 working days and will be communicated to you via the screening team/Mr Maher.

Consultant Obstetrician

harmony
PRENATAL TEST
performed in the UK

Roche

TDL GENETICS

The Halo Building
1 Mabledon Place
London
WC1H 9AX

T: +44 (0) 20 7307 7409
E: [illegible]

www.tdlpathology.com

Patient and Provider Information

PATIENT NAME: [redacted]	ACCOUNT #: EASTLANC
DATE OF BIRTH: (DD/MM/YYYY) [redacted]	CLINIC NAME: East Lancashire Hospitals Trust
MRN: [redacted]	REFERRING/ORDERING CLINICIAN: [redacted]
LABORATORY ID: [redacted] OTHER ID:	REFERRING/ORDERING CLINICIAN EMAIL: [redacted]
GESTATIONAL AGE: 13 wks 3 days	OTHER CLINICIAN:
# OF FETUSES: 1 IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN CONTACT INFORMATION:
COLLECTION DATE (DD/MM/YYYY): 29/03/2019 RECEIVED DATE (DD/MM/YYYY): 01/04/2019	REPORT DATE: (DD/MM/YYYY) 04/04/2019

Test Results

Fetal cfDNA Percentage: 21%

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.

Fetal Sex test quantifies the Y chromosome. A "female" result indicates no detection of Y chromosome and a "male" result indicates detection 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 VALIDATION DATA FROM THE HARMONY PRODUCT INSERT*

	Detection Rate	False Positive Rate
T21	107/108	0/641
T18	29/29	0/641
T13	12/12	0/641

Detection and false positive [illegible] based on probability cutoff of 1/100 (1%). Because these conditions are rare, limited numbers of aneuploidy twin 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: [illegible] accuracy for male or female sex.

SCA Panel: 15/15 detection rate; false positive rate 3/[illegible].

*REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4. [illegible] Harmony [illegible] Instructions for Use. Clinical data based on a sample set analysed with microarray quantitation. Performance results may vary based on the laboratory performing the test.

PTR-1402 Rev 3.0

NHS
East Lancashire Hospitals
NHS Trust
Lancashire Women & Newborn Centre
Casterton Avenue
Burnley
BB10 2PQ

Hospital No
NHS No.:
Date 16/04/2019

Genetic Counselling

Patient:

Exam date:

Indication	Maternal request
Pregnancy	Singleton pregnancy. Number of fetuses: 1.
Test Results	Please find enclosed the results of your recent Harmony Non-Invasive Prenatal Test (NIPT).
	The results indicate that you are LOW PROBABILITY for Trisomy 21 (Down Syndrome), Trisomy 18 (Edward Syndrome) and Trisomy 13 (Patau Syndrome).
	The fetal sex was determined to be MALE.
	The amount of fetal cells within the blood test was deemed sufficient to analyse the sample (fetal fraction 9.7%).
	As you recall, we discussed that the NIPT is not a diagnostic test so will not detect all cases of chromosome problems. Only invasive tests (amniocentesis) are diagnostic at this stage. If you wish to proceed with an invasive test at this stage please contact the screening team.
	The test will not detect mosaicism, partial chromosome problems, translocations or maternal chromosomal problems. Harmony does not detect structural problems with your baby - these are best detected at your 20-week anomaly scan.
Follow-up	No further screening tests have been arranged at this stage.
	If you wish to proceed with an invasive test (amniocentesis) please contact the screening midwives on the number above and they will arrange this for you in the Fetal Medicine

Unit.

If you wish to discuss the test any further please feel free to contact my secretary on 01282-803197.

Consultant Obstetrician

CC:

East Lancashire Hospitals
NHS Trust
Lancashire Women & Newborn Centre
Casterton Avenue
Burnley
BB10 2PQ

Hospital No:
NHS No.:
Date 10/6

Genetic Counselling

Patient:

Exam date:

Indication	Maternal request
Pregnancy	Singleton pregnancy. Number of fetuses: 1.
Counselling Summary	Attended for Non-Invasive Prenatal Testing (NIPT) due to maternal request

Explained that this is a private test not available on NHS at present.
Harmony is the company of choice in ELHT, but other providers are available privately. Cost of the test is £350 (Harmony will invoice you for this directly).

Discussed that screening for fetal chromosomal disorders is optional. Implications for the test results discussed. The decision to proceed is based on how each individual perceives the benefits of obtaining the information about chromosomal problems when weighed against the potential emotional and physical risks of testing.

NIPT is a screening test. It cannot diagnose or eliminate the chance that a fetus has a particular chromosomal condition; rather it separates women into high and low risk categories. Testing is performed using a blood test of mother from the arm and is not associated with an increased risk of miscarriage.

We discussed that the only diagnostic test at this gestation is an amniocentesis test. This is a test where a small needle is placed through your abdomen under ultrasound guidance and a small amount of fluid surrounding the baby is taken for analysis. This will confirm if the baby is affected by a chromosomal condition. There is a small risk of 0.5-1% of miscarriage.

Clinical features of each condition screened for in the test discussed. These included:

- Trisomy 21 (Down Syndrome)
- Trisomy 18 (Edwards Syndrome)
- Trisomy 13 (Patau Syndrome)
- Sex chromosome aneuploidies (monosomy X, XXY, XXX, XYY) . The test for this is optional. You decided that you did not want to proceed with this test.
- Sex of the fetus. This test is optional. You have expressed that you wish this test to be performed.

Specific testing methods discussed – there are fragments of chromosomes that circulate outside of cells within the mothers blood. These DNA fragments are referred to as 'cell-free'. Most cell free DNA fragments derive from the mothers blood cells, but some come from the placenta. Because the fetus and placenta derive from the same fertilised cell, they are usually genetically identical. The sequences of cell free DNA fragments are analysed to establish how many fragments there are and which chromosomes they have come from. The laboratory counts the number of fragments from each chromosome of interest, and determines if there are more or less than expected. If, for example, there are more than expected number of fragments from chromosome 21, this indicates an increased chance of the baby having trisomy 21.

The results will be communicated from the test laboratory to East Lancashire Hospitals and communicated to you once this has been received. A result is normally available in 3-5 working days, but can sometimes be longer than this. If you do not hear anything back after 7 working days please contact Mr Maher's secretary or the screening team.

In 3 out of 100 women a repeat test will be required (a result is achieved in approximately two thirds of these). This is because the amount of fetal blood cells in your circulation is not enough for the laboratory to test. This is called the fetal fraction. If the test requires repeating you will not be charged for this.

NIPT is not diagnostic but a screening test. This means that the test has a certain sensitivity for each condition and can sometimes be wrong.
We discussed the sensitivity for Trisomy 21 is over 99% (false positive rate <0.1%)
Trisomy 18 is 97.4% (false positive rate <0.1%)
Trisomy 13 is 93.8% (false positive rate <0.1%)
I explained that the result will give a high or low risk result. If you wish to consider invasive/diagnostic tests following the results these can be arranged in the Fetal Medicine Unit.

Following counselling today, you wished to proceed with the test and written consent was obtained for this.
Ultrasound scan confirms a viable pregnancy.
Blood samples have been taken today using an aseptic non-touch technique and sent by recorded mail to the Harmony laboratory.

Follow-up Results will normally be available in 3-5 working days and will be communicated to you via the screening team/Mr Maher.

Consultant Obstetrician

harmony
PRENATAL TEST
performed in the UK

Roche

TDL GENETICS
The Halo Building
1 Mabledon Place
London
WC1H 9AX

T: +44 (0) 20 7207 7409
E: [redacted]
www.tdlpathology.com

Patient and Provider Information

PATIENT NAME:	ACCOUNT #: EASTLANC
DATE OF BIRTH: (DD/MM/YYYY)	CLINIC NAME: East Lancashire Hospitals Trust
MRN:	REFERRING/ORDERING CLINICIAN: [redacted]
LABORATORY ID: [redacted]	REFERRING/ORDERING CLINICIAN EMAIL: [redacted]
GESTATIONAL AGE: 14 wks 2 days	OTHER CLINICIAN:
# OF FETUSES: 1	IVF STATUS: non-IVF pregnancy
COLLECTION DATE (DD/MM/YYYY): 10/04/2019	RECEIVED DATE (DD/MM/YYYY): 11/04/2019
OTHER ID:	OTHER CLINICIAN CONTACT INFORMATION:
	REPORT DATE: (DD/MM/YYYY) 15/04/2019

Test Results

Fetal cfDNA Percentage: 9.7%

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

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.

Fetal Sex test quantifies the Y chromosome. A "female" result indicates no detection of Y chromosome and a "male" result indicates detection of Y chromosome. It does not exclude sex chromosome aneuploidy. For twin pregnancies, a male result indicates one or two male fetuses.

CLINICAL VALIDATION DATA FROM THE HARMONY PRODUCT INSERT*

	Detection Rate	False Positive Rate
T21	107/108	0/641
T18	20/20	0/641
T13	11/12	0/641

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

Fetal Sex: 268/287 accuracy for male or female fetus

*REFERENCES: Sarkozy A et al. Prenatal Diagnosis 2015; 35:1-4. IFU-1200 Harmony IVD Kit Instructions for Use. Clinical data based on a sample set analyzed with manual examination. Performance results may vary based on the laboratory performing the test.

NHS
East Lancashire Hospitals
NHS Trust
Lancashire Women & Newborn Centre
Casterton Avenue
Burnley
BB10 2PQ

Hospital No:
NHS No.:
Date 30/04/2019

Genetic Counselling

Patient: IE

Exam date:

Indication Raised risk on combined screening

Pregnancy Singleton pregnancy. Number of fetuses: 1.

Test Results Please find enclosed the results of your recent Harmony Non-Invasive Prenatal Test (NIPT).

The results indicate that you are HIGH PROBABILITY for Trisomy 21 (Down Syndrome)and LOW PROBABILITY for Trisomy 18 (Edward Syndrome) and Trisomy 13 (Patau Syndrome).

The fetal sex was determined to be male.

The amount of fetal cells within the blood test was deemed sufficient to analyse the sample (fetal fraction 16.2%).

As you recall, we discussed that the NIPT is not a diagnostic test so will not detect all cases of chromosome problems. Only invasive tests (amniocentesis) are diagnostic at this stage. If you wish to proceed with an invasive test at this stage please contact the screening team.

The test will not detect mosaicism, partial chromosome problems, translocations or maternal chromosomal problems. Harmony does not detect structural problems with your baby - these are best detected at your 20-week anomaly scan.

Follow-up In view of the raised probability result an appointment has been made for you with the screening team/Fetal Medicine Unit to discuss this further and discuss any further investigations that you may wish to consider.

If you wish to discuss the test any further in the meantime please feel free to contact my secretary on 01282-803197.

Consultant Obstetrician

CC:

harmony
PRENATAL TEST
performed in the UK

TDL GENETICS

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1 Mabledon Place
London
WC1H 9AX

T: +44 (0) 20 7307 7409
E: [illegible]

www.tdlpathology.com

Roche

HIGH PROBABILITY RESULT

Patient and Provider Information

PATIENT NAME: [redacted]	ACCOUNT #: EASTLANC
DATE OF BIRTH: (DD/MM/YYYY)	CLINIC NAME: East Lancashire Hospitals Trust
MRN:	REFERRING/ORDERING CLINICIAN: [redacted]
LABORATORY ID: [redacted] OTHER ID:	REFERRING/ORDERING CLINICIAN EMAIL: [redacted]
GESTATIONAL AGE: 13 wks 3 days	OTHER CLINICIAN:
# OF FETUSES: 1 IVF STATUS: non-IVF pregnancy	OTHER CLINICIAN CONTACT INFORMATION:
COLLECTION DATE (DD/MM/YYYY): 18/04/2019 RECEIVED DATE (DD/MM/YYYY): 23/04/2019	REPORT DATE: (DD/MM/YYYY) 29/04/2019

Test Results

Fetal cfDNA Percentage: 16.2%

CHROMOSOME	RESULT	PROBABILITY	RECOMMENDATION
Trisomy 21 (T21)	High Probability	Greater than 99/100 (99%)	Genetic counselling 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

Fetal Sex	Male

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.

Fetal Sex test quantifies the Y chromosome. A "female" result indicates no detection of Y chromosome and a "male" result indicates detection of Y chromosome. It does not exclude sex chromosome aneuploidy. For twin pregnancies, a male result indicates one or two male fetuses.

CLINICAL VALIDATION DATA FROM THE HARMONY PRODUCT INSERT*

	Detection Rate	False Positive Rate
T21	107/108	0/641
T18	29/29	0/641
T13	12/12	0/641

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 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: [illegible] accuracy for male or female sex.

*REFERENCES: Stokowski R et al. Prenatal Diagnosis 2015; 35, 1-4; IFU-2290 Harmony IVD Kit instructions for use. Clinical data based on a sample set analysed with microarray quantitation. Performance results may vary based on the laboratory performing the test.

The Harmony Prenatal Test® was developed by Ariosa Diagnostics (San Jose, California, USA). The Harmony® reagents and Ariosa cell-free DNA System (ACS) software used as part of the Harmony Prenatal Test are CE Marked under the IVD Directive 98/79/EC. Harmony is a non-invasive prenatal test (NIPT) based on cell-free DNA analysis. The results are intended for prenatal screening and are not intended to be the sole basis for diagnosis. 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.

PTR-1402 Rev 3.0

Qd

East Lancashire Hospitals
NHS Trust
Lancashire Women & Newborn Centre
Casterton Avenue
Burnley
BB10 2PQ

Hospital No:
NHS No.:
Date

Genetic Counselling

Patient:

Exam date:

Indication	Maternal request, Raised risk on combined screening
Pregnancy	Singleton pregnancy. Number of fetuses: 1.
Counselling Summary	Attended for Non-Invasive Prenatal Testing (NIPT) due to an increased chance result on the combined test for T21.

Explained that this is a private test not available on NHS at present.
Harmony is the company of choice in ELHT, but other providers are available privately. Cost of the test is £350 (Harmony will invoice you for this directly).

Discussed that screening for fetal chromosomal disorders is optional. Implications for the test results discussed. The decision to proceed is based on how each individual perceives the benefits of obtaining the information about chromosomal problems when weighed against the potential emotional and physical risks of testing.

NIPT is a screening test. It cannot diagnose or eliminate the chance that a fetus has a particular chromosomal condition; rather it separates women into high and low risk categories. Testing is performed using a blood test of mother from the arm and is not associated with an increased risk of miscarriage.

We discussed that the only diagnostic test at this gestation is an amniocentesis test. This is a test where a small needle is placed through your abdomen under ultrasound guidance and a small amount of fluid surrounding the baby is taken for analysis. This will confirm if the baby is affected by a chromosomal condition. There is a small risk of 0.5-1% of miscarriage.

Clinical features of each condition screened for in the test discussed. These included:
- Trisomy 21 (Down Syndrome)
- Trisomy 18 (Edwards Syndrome)
- Trisomy 13 (Patau Syndrome)
- Sex chromosome aneuploidies (monosomy X, XXY, XXX, XYY) . The test for this is optional. You decided that you DID NOT want to proceed with this test.
- Sex of the fetus. This test is optional. You have expressed that you wish this test to be performed.

Specific testing methods discussed – there are fragments of chromosomes that circulate outside of cells within the mothers blood. These DNA fragments are referred to as 'cell-free'. Most cell free DNA fragments derive from the mothers blood cells, but some come from the placenta. Because the fetus and placenta derive from the same fertilised cell, they are usually genetically identical. The sequences of cell free DNA fragments are analysed to establish how many fragments there are and which chromosomes they have come from. The laboratory counts the number of fragments from each chromosome of interest, and determines if there are more or less than expected. If, for example, there are more than expected number of fragments from chromosome 21, this indicates an increased chance of the baby having trisomy 21.

The results will be communicated from the test laboratory to East Lancashire Hospitals and communicated to you once this has been received. A result is normally available in 3-5 working days, but can sometimes be longer than this. If you do not hear anything back after 7 working days please contact Mr Maher's secretary or the screening team.

In 3 out of 100 women a repeat test will be required (a result is achieved in approximately two thirds of these). This is because the amount of fetal blood cells in your circulation is not enough for the laboratory to test. This is called the fetal fraction. If the test requires repeating you will not be charged for this.

NIPT is not diagnostic but a screening test. This means that the test has a certain sensitivity for each condition and can sometimes be wrong.
We discussed the sensitivity for Trisomy 21 is over 99% (false positive rate <0.1%)
Trisomy 18 is 97.4% (false positive rate <0.1%)
Trisomy 13 is 93.8% (false positive rate <0.1%)
I explained that the result will give a high or low risk result. If you wish to consider invasive/diagnostic tests following the results these can be arranged in the Fetal Medicine Unit.

Following counselling today, you wished to proceed with the test and written consent was obtained for this.
Ultrasound scan confirms a viable pregnancy.
Blood samples have been taken today using an aseptic non-touch technique and sent by recorded mail to the Harmony laboratory.

Follow-up Results will normally be available in 3-5 working days and will be communicated to you via the screening team/Mr Maher.

Consultant Obstetrician