REQUEST FORM: NON-INVASIVE PRENATAL TEST (NIPT)

SAMPLE INFORMATION	
Hospital or laboratory Label	Strict preanalytical conditions apply (see below) Date Time

LNS BARCODE LABEL
LNS label

LNS LUXEMBOURG

LABORATOIRE NATIONAL DE SANTE
NATIONAL CENTER OF GENETICS

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Forms available at www.lns.lu

PHYSICIAN REQUESTING THE TEST

Surname and first name of the prescriber

Address and country

Telephone / direct line

Fax

Date of request

Signature / Stamp

PATIENT

Maiden name

First name

Married surname

Sex

Date of birth

National identification number

Address and country

Patient covered by the CNS ☐ Yes ☐ No

*If not covered by the CNS, the patient will receive an invoice from the laboratory, which they may pass on to their insurance company, where applicable.

Copies to be sent to [Only the doctor/healthcare professional who has requested the test may give the results to the patient.]

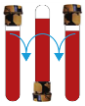
BLOOD SAMPLE: PREANALYTICAL CONDITIONS

The mother's blood must be collected in **1 Streck tube**.

Take 1 STRECK tube

Fill the tube

Invert 10 times



Transport: Temperature and duration

May be kept at ambient temperature for a maximum period of 72 hours

PATIENT INFORMATION (The date of the beginning of the pregnancy and the Number of Embryos are mandatory)

Personal details:

Patient Age | Pre-pregnancy weight ..... kg | Height | BMI

If the patient's BMI is >35, taking the sample at 16 weeks of gestation onwards reduces the risk of a 'no call' result due to low foetal fraction (Livergood et al., AJOG, supplement 2017).

Relevant personal or family history: .....

Type of pregnancy: ☐ natural ☐ IVF

Date of beginning of pregnancy or expected date of delivery: (determined by measuring CRL, except in the case of ART) : .....

12-week ultrasound scan: (or attach report)

☐ Not performed
☐ No abnormalities found on ultrasound scan
☐ Abnormalities found on ultrasound scan, please specify:..... (or attach report)

Number of embryos:

☐ Singleton pregnancy: CRL: ..... mm NT: ..... mm
☐ Vanishing twin
☐ Twin pregnancy (☐ Dichorionic - Diamniotic ☐ Monochorionic - Diamniotic ☐ Monochorionic - Monoamniotic)
Twin 1 (twin A): CRL: .....mm NT: .....mm Twin 2 (twin B): CRL: .....mm NT: .....mm

Treatments or clinical situations which may affect the result:

☐ Not receiving any treatment known to interfere with NIPT
☐ Low-molecular-weight heparin (LMWH)
If the patient is receiving LMWH, it is recommended that the NIPT sample is taken just before a heparin injection is given (Grömminger et al., Prenatal Diagnosis, 2015).
☐ Blood transfusion
☐ Organ transplant, stem cell transplant or bone marrow transplant
☐ Cancer
☐ Immunotherapy

CLINICAL INFORMATION

PLEASE NOTE: this test is not recommended when nuchal translucency is >3.5 mm or when other abnormalities have been identified on the ultrasound scan. The test should be performed ideally after 12 weeks of gestation and following the 12-week ultrasound scan and never before 10 weeks of gestation.

☐ low-risk population screening
☐ Specific clinical situation:.....
☐ Age of mother >35 years
☐ Maternal serum marker screening risk >1/1000 (please attach report)
☐ Previous pregnancy with aneuploidy – in the patient or a 1st degree relative (Please specify):.....
☐ Balanced Robertsonian translocation in one of the parents involving chromosome 13 or 21 (please attach the parent's karyotype)

Please specify: ..... (or attach report)
☐Other (please contact the laboratory): .....

INFORMATION FOR PATIENTS ON NON-INVASIVE PRENATAL TESTING (NIPT)

What is NIPT?

Non-invasive prenatal testing (NIPT) is a genetic test that screens for the most common chromosomal abnormalities in foetuses, including trisomies 21, 18 and 13. One of the aims of the test is to minimise the number of invasive procedures.

This method is based on the sequencing of free-floating DNA, called cell-free fetal DNA (cffDNA), in the mother's blood. Cell free DNA consists mainly of DNA from the mother's cells, but also contains DNA from the placental cells (cytotrophoblasts), which reflect the chromosomal make-up of the foetus. High-throughput sequencing allows to accurately quantify cffDNA and thus to assess whether an extra chromosome 21 (trisomy 21), chromosome 13 (trisomy 13) or chromosome 18 (trisomy 18) is present in the foetus. NIPT is a screening method that cannot exclude the presence of trisomy 13, 18, 21 in the foetus with 100% certainty even, if the NIPT result is negative. More details on the performance of the method are available on our website: https://lns.lu/departement/genetique/nipt/

The NIPT test is very reliable. Both the analytical sensitivity and specificity are greater than 99.9% for trisomies 13, 18 and 21 (*basic screening for singleton pregnancies, data: Illumina. Results from the Veriseq NIPT Solution v2 clinical validation study*).

How does the test work in practice?

The patient is free to decide whether to do NIPT testing or not. NIPT can only carried out after your 12-week ultrasound scan. Nuchal translucency must be normal. NIPT may be requested by your doctor or any healthcare professional able to request it, ideally after **12 weeks of gestation and not before 10 weeks of gestation.**

The test must be requested following a consultation during which you will have had the chance to ask your healthcare professional any questions you may have about the test. That way, you can make an informed decision based on the knowledge of the test reliability and limitations. The doctor/healthcare professional who has requested the test will ask you to provide written consent for the test. NIPT is done using a blood sample. The result of your NIPT will be sent only to the doctor/healthcare professional who has requested the test and never to you directly. NIPT is currently free of charge for patients covered by the CNS.

Results

Results are usually sent out in 10 days to the doctor/healthcare professional who has requested the test.

- **If the result is negative**: this means that the amount of foetal DNA from chromosome 21, 18 and 13 is normal and that foetal trisomy 21, 18 or 13 is very unlikely. The pregnancy should be monitored as planned.
- **If the result is positive**: this means the amount of foetal DNA from chromosome 21, 18 or 13 is abnormally high and there is a high probability that the foetus has trisomy 21, 18 or 13. A diagnostic test to confirm the result should be performed. This involves analysing the foetal chromosomes based on an amniotic fluid sample (more rarely a chorionic villus sample). Both are invasive procedures, which carry a low risk of miscarriage (0.1-0.5% of patients).
- **Inconclusive result**: on rare occasions (<0.5% of patients), a reliable result cannot be obtained. Depending on your clinical situation, you may be advised to repeat the test.
- **Additional findings**: in rare cases, NIPT may reveal chromosomal abnormalities implicating chromosomes other than 13,18 and 21 which were not initially being screened for. Those are so called additional findings. In such a case, you will be advised to attend a genetic consultation. During that consultation, you will be informed about the type of abnormality that has been identified, how it will affect the foetus and/or mother and any additional tests which may need to be performed.

Limitations of NIPT

NIPT has certain limitations:

- Technical failures are possible, especially if the test is done too early in the pregnancy, (i.e. before 10 weeks of gestation), in patients taking low molecular weight heparin and in patients with a body mass index -BMI of >35. In such cases, we may recommend to repeat the test or, depending on your clinical situation, to use an invasive procedure for the detection of foetal chromosome abnormalities.
- Although NIPT is very reliable, there are very rare cases of false positives. In particular the abnormality can be present in the placenta but not in the foetus (cffDNA is derived from the placenta). This is the reason why every positive NIPT result should be confirmed by means of foetal karyotyping on amniotic fluid.
- There are also very rare cases of false negatives, where the abnormality is present in the foetus but not in the placenta. This is why NIPT is not a substitute for foetal karyotyping or prenatal ultrasound scans.
- The reliability of NIPT can be reduced in multiple pregnancies.

NIPT does not replace foetal karyotyping and is not intended for the screening of unbalanced chromosomal abnormalities: microdeletions, micro duplications.,. It is not intended for the detection of balanced chromosomal abnormalities (translocations, inversions), mosaic chromosomal abnormalities, point mutations or other genetics events underlying monogenic disorders. Pregnancy follow-up, particularly ultrasound monitoring should be carried out as as planned.

CONSENT

I have understood the degree of reliability and limitations of NIPT. I have had the opportunity to ask my doctor any questions I have on this screening test and these have been answered in a clear and satisfactory manner. I understand and agree that my personal data is being stored for medical purposes only. I understand that the test may result in incidental findings.

Based on the above, I hereby consent to having NIPT performed under the conditions outlined above to screen for pathogenic chromosomal aneuploidies in my foetus.

I would like to know the sex of my foetus.	☐ Yes ☐ No
I consent that my sample and my personal data may be used (anonymously) for the purpose of clinical research, confirmatory testing or method validation by the laboratory.	☐ Yes ☐ No

Patient Signature

Date and Place: ……

Signature: ……

Physician Signature

Date and Place: ……

Signature: ……