Niptify®
Non-Invasive Prenatal screening Test (NIPT)

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INFORMED CONSENT

NIPTIFY Focus Plus is a CE-IVD marked screening test assessing fetal chromosomal disease risk from 10+ weeks of gestation. For the analysis, up to two tubes of venous blood are taken from the pregnant woman. The test is clinically validated to evaluate the risk of trisomy of chromosomes 13 (**Patau syndrome**), 18 (**Edwards syndrome**), 21 (**Down syndrome**), absence of one X chromosome in a female fetus (**Turner syndrome** or monosomy X), and microdeletion 22q11 (**DiGeorge syndrome**) in the fetus. If desired, the chromosomal **sex of the fetus** is determined.

The sensitivity of the NIPTIFY test is greater than 99.9% for trisomies 21, 18, and 13, monosomy X and 22q11 microdeletion*. The test's specificity is more than 99.9% for trisomies 21 and 18 and microdeletion 22q11. The test's specificity is 99.2% for monosomy X and trisomy 13.

GENOME-WIDE STUDY and INCIDENTAL FINDINGS

NIPTIFY performs a genome-wide study and has the power to identify copy-number variances in entire chromosomes (**trisomies** or **monosomies**) and deletions and duplications in clinically significant regions (**microdeletions** or **microduplications**). There are four types of conditions under analysis: trisomy or monosomy in autosomal chromosomes other than 13, 18, 21; segmental aneuploidies in chromosomes 13, 18, 21; **sex chromosome aneuploidies** like Klinefelter (XXY), Jacobs (XYY), trisomy X (XXX) syndromes; clinically significant regions for possible microdeletions and microduplications. NIPTIFY reports such cases as **incidental findings ONLY IF** a high risk of the condition is detected. Incidental findings are not clinically validated. Homepage **NIPTIFY.com/results** provides detailed information about the regions and conditions.

RESULTS

The NIPTIFY results are sent to the clinician no later than 10 working days after the blood sample arrives at the Competence Centre on Health Technology (NIPTIFY) laboratory. The test result and the need for subsequent analysis must be explained to the patient by a doctor, midwife, or medical geneticist. The test can give four different results:

Low risk. The result shows that no trisomy 13, 18, 21, monosomy X, 22q11 microdeletion was detected in the sample. The probability that the fetus will have a chromosomal disorder is very low. The pregnancy is considered 'normal' and monitored regularly.

High risk. The result shows that the fetus has a high probability of trisomy 13, 18, or 21, monosomy X, 22q11 microdeletion. Patients with a high-risk result should be counseled by a doctor or medical geneticist, who will make decisions with the patient about the additional tests needed. Decisions about the subsequent course of the pregnancy should not be made based on the NIPTIFY results alone. An invasive diagnostic test (amniocentesis) should confirm high-risk chromosomal disease results.

Incidental findings. The fetus has been identified as being at high risk for other chromosomal diseases. In this case, the patient must be advised by a doctor or medical geneticist, who together with the patient will make decisions about the additional tests. Decisions about the subsequent course of the pregnancy should not be made based on the NIPTIFY result alone, because a high risk should be confirmed by ultrasound or an invasive diagnostic test (amniocentesis).

Unable to determine. Based on the blood sample, it is not always possible (less than 0.5%) to reliably assess the risk of chromosomal diseases. The patient has the option to give a new blood sample for the NIPTIFY retesting. One retest is free for the patient. More information can be found at **NIPTIFY.com**

METHODS

During the NIPTIFY test, cell-free DNA isolated from a pregnant woman's blood sample is analyzed with the Focus Plus method (*Fragmented DNA Compact Sequencing Assay for enriched fetal material*) and sequenced with Illumina technology. Risk estimates for fetal chromosomal diseases from placental origin genomic material are calculated based on whole genome data.

RISKS AND LIMITATIONS ARISING FROM THE METHODOLOGY

NIPTIFY does not substitute ultrasound, or serum screening and is not a diagnostic test. Therefore, the possibility of false-negative or false-positive results remains. The test can give false results for various clinical reasons such as placental or maternal mosaicism, chromosomal abnormalities if the mother has a tumor, the mother is a carrier of a studied aneuploidy, or other biological and technical reasons. A test result with a low risk of chromosomal disease does not exclude other abnormalities of fetal development detected by ultrasound examination. NIPTIFY does not provide information about fetal developmental disorders such as brain or heart developmental disorders, spine developmental disorders, fetal growth disorders, etc. NIPTIFY is not validated to detect mosaicism, balanced translocations, and monogenic point mutation diseases. The NIPTIFY test cannot be performed in multiple pregnancies or if the patient has been diagnosed with a malignancy during the current pregnancy. More information can be found at **NIPTIFY.com**

* The sensitivity of determining the DiGeorge microdeletion (22q11) has been validated based on a limited number of control samples. Based on the scientific literature, the expected sensitivity of the NIPT test for 22q11 determination is 75-100%.

I confirm that I have read the information on the consent form and I agree to give a blood sample for the NIPTIFY test.

.....
First name and surname of the patient

....
Signature Date

TEST ORDERING FORM

Sample ID

Single pregnancy? ☐ YES

Do we report the sex of the fetus? ☐ YES ☐ NO

Are you repeating this test for the second time? ☐ YES ☐ NO

Does patient have a malignant tumor? ☐ YES ☐ NO

Clinician's name

Clinician's phone number

Clinician's e-mail

Send results to e-mail

First name and surname of the patient

Date of birth (dd/mm/yyyy) | Gestational age (weeks)

Height (cm) | Weight (kg)

Date of blood sampling (dd/mm/yyyy)

Notes

☐ I confirm that I am ordering the NIPTIFY Focus Plus test at the patient's request. The test evaluates the risks of fetal trisomy of 13, 18, and 21 chromosomes, DiGeorge (22q11) microdeletion syndrome, monosomy X (45,X), and determines fetal chromosomal sex. I confirm that the patient has been informed about the possible results, risks, and limitations of the NIPTIFY Focus Plus test. I confirm that here presented data is correct.

☐ If a high risk is detected, I confirm the patient's request to report **incidental findings** under the terms described in the Informed Consent.

.....
Clinician's signature

The document is in **THREE copies**. The clinician keeps one, another is for the patient, and the third is packed with blood sample and shipped to the laboratory.