DOCUMENT OF COMPLEMENTARY DATA

NIDA®

NON INVASIVE PRENATAL TESTING FOR ANEUPLODIES DETECTION (CHROMOSOMES 21, 18, 13, X, Y)

PATIENT DATA

LAST NAME _____

FIRST NAME _____ ID No. _____

DATA OF CURRENT PREGNANCY

GESTATIONAL AGE:

BY LAST MENSTRUAL PERIOD (LPM): ____ BY ULTRASOUNDS: _____

COMBINED INDEX RISK:

T21: _____ T18: _____

SPECIFY: ☐ SINGLE PREGNANCY ☐ TWINS PREGNANCY

IDENTIFICATION LABEL
(by GENYCA)

CLINICAL HISTORY

TOTAL No. of PREGNANCIES including the current one, abortions, trophoblastic diseases (choriocarcinoma and moles) and ectopic. _____

No. of TERM PREGNANCIES: _____ No. of PREMATURE PREGNANCIES: _____

No. of ABORTIONS AND ECTOPIC PREGNANCIES: _____ IN CASE OF PREVIOUS ABORTION, DATE: _____

No. of DESCENDANTS CURRENTLY ALIVE: _____

FAMILY MEDICAL HISTORY OF TRISOMIES: _____

FAMILY MEDICAL HISTORY OF OTHER GENETIC DISEASES (specify):

_____

_____

INFORMATION ABOUT THE TEST

Until recently, the chromosomal health of the fetus could be verify through noninvasive biochemical markers in the mother and / or ultrasonography (ultrasounds) or by invasive screening tests such as amniocentesis, cordocentesis or chorionic villus sampling, which increase the risk of fetal loss. It is now possible to perform a non-invasive prenatal chromosomal analysis **without any risk to the fetus and with a high sensitivity.**

Numerical abnormalities (aneuploidies) of chromosomes 21, 13, 18 and sexual chromosomes (X and Y) are the most frequent chromosomal abnormalities prenatally detected. The trisomy of chromosome 21 that causes Down's syndrome is the most common chromosomal disorder and is characterized by the presence of three copies of this chromosome. Down syndrome has an incidence of approximately 1 in 800 births and is associated with mental retardation and multiorganic abnormalities. The trisomy of chromosome 13 (Patau Syndrome) and 18 (Edwards Syndrome) course with a multiple severe malformations, with high rates of perinatal death and a frequency of approximately 1 per 5000 births. The sex chromosome aneuploid cells have a prevalence of 1 per 300-400 births.

Non-invasive prenatal testing is based on the analysis of fetal DNA free in maternal peripheral blood. The fetal DNA fraction usually represents <10% of total DNA in maternal plasma[1] and it is correlated with gestational age[2].
NIDA analyzes the free fetal DNA using next-generation sequencing MPSS (Massively Parallel Shotgun Sequencing), in order to estimate the **risk probability of developing fetal aneuploidies of chromosomes 21, 13, 18, X or Y.**

All the validation studies published to date have demonstrated the high reliability of this noninvasive test, according to data collected in the following table:

	Trisomy21[4]	Trisomy 18[5]	Trisomy 13[5]	X0[6]	XXY[6]	XYY[6]
Sensibility	100%	92%	100%	75%	100%	100%
Specifity	97,9%	98%	98,9%	99,9%	100%	100%

Sensitivity: indicates the percentage of correctly identified cases with trisomy.
Specificity: indicates the percentage of correctly identified cases without trisomy.

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Since this is not a diagnostic test, but an **advanced screening test** (ISPD, International Society for Prenatal Diagnosis) [3], in cases reported as high risk a confirmation of the result is recommended by performing an invasive diagnostic test (as QF-PCR or fetal karyotype). NIDA not detect structural chromosomal abnormalities or aneuploidy of chromosomes other than those studied (21, 18, 13, X and Y), therefore the result should be evaluated by the specialist as clinical reference in the context of other data from the mother. Likewise, and despite being a test with a specificity> 99%, a low probability of trisomy does not completely exclude the possibility of existence of fetal trisomy.

Different conditions can affect the accuracy of NIDA, causing false positives or false negatives[7,8]:

- In cases of insufficient fraction of free fetal DNA, or due to gestational age below 12 weeks (by ultrasounds) at the time of sampling, or in cases of maternal excessive weight gain.
- If the mother has recently received an allogeneic blood transfusion, or a transplantation or stem cell therapy.
- If case of fetal mosaicism, triploidy, or chromosomal microdeletion or microduplication.
- When the mother suffers from trisomy for any of the analyzed chromosomes, constitutional or acquired mosaicism for any aneuploidy, or a malignant cancerous process.
- In cases of vanishing twin syndrome.
- In the presence of placental mosaicism.

If the sample received at the laboratory is in poor condition, or that a a reportable result may not be obtained after the processing of the provided sample (0.5-7% of cases, depending on the laboratory), the specialist prescribing the test, together with the patient and geneticists specialized in this type of testing, will appreciate the convenience of repeating the test from a new sample, try other diagnostic approaches, or decline any further testing.

By the signature of the present document, the reception of specific information related to the study NIDA and the veracity of the data provided by the person undersigning this document are both confirmed.

NAME OF THE PERSON SIGNING _____

If the patient is minor or requests legal representation for any other reason, detail the RELATIONSHIP TO THE PATIENT (by presentation of the official document proving the relationship and personal identity document): _____

ID No. _____ DATE _____

SIGNATURE:

REFERENCES

1. Lo et al., 1998. Quantitative analysis of fetal DNA in maternal plasma and serum: implications for noninvasive prenatal diagnosis. Am J Hum Genet 62:768-775
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3. ISPD (International Society for Prenatal Diagnosis), Rapid Response Statement 24 October 2011
4. Chiu RW et al., 2011. Non-invasive prenatal assessment of trisomy 21 by multiplexed maternal plasma DNA sequencing: large scale validity study. BMJ 342:c7401
5. Chen EC et al., 2012. Noninvasive prenatal diagnosis of fetal trisomy 18 and trisomy 13 by maternal plasma DNA sequencing. PLoS ONE e21791
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8. Mennuti et al., 2013. Is it time to sound an alarm about false-positive cell-free DNA testing for fetal aneuploidy?. Am J Obstet Gynecol 209(5):415-419

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