CentoNIPT® — Information Sheet

Dear Patient,

Your physician recommends a non-invasive prenatal testing ("**CentoNIPT®**") for you or the patient for whom you are the custodian or legal guardian (hereinafter, "**you**" or "**the Patient**").

CENTOGENE shall only perform the non-invasive prenatal testing. It remains the sole responsibility of the treating physician to interpret the result(s) of such non-invasive prenatal testing and to inform you or the Patient of the results of the genetic testing.

In the following we shall inform you or the Patient about the testing procedure, possible results, and potential risks. You or the Patient may wish to consult with a genetic counselor before signing the Informed Consent Form.

CentoNIPT screens for some chromosomal disorders in unborn children. During pregnancy, maternal blood contains genetic material, so called cell-free DNA (cfDNA), both from the mother as well as from the fetus. DNA encodes the relevant genetic information necessary for the development, function, growth and reproduction of humans. Chromosomal abnormalities can compromise the developing fetus as a result of incorrect processing of the genetic material in egg or sperm formation and/or during the earliest stages of the fetus' development. These chromosomal abnormalities can significantly affect the health and well-being of the newborn.

The biological material ("**Sample**") required for CentoNIPT is maternal blood.

CentoNIPT screens for:
- **Down syndrome** (Trisomy 21): affects 1 in 1,000 live births
- **Edwards syndrome** (Trisomy 18): affects 1 in 3,000 – 6,000 live births
- **Patau syndrome** (Trisomy 13): affects 1 in every 5,000 live births
- **Turner syndrome** (Monosomy X)
- **Klinefelter syndrome** (XXY)
- **Jacobs syndrome** (XYY)
- **Triple X syndrome** (XXX)

As CentoNIPT includes analysis of the sex chromosomes, you can also find out the gender of the fetus. CentoNIPT is also suitable if you or the Patient are/is pregnant with twins.

Possible Results and Significance of the Results
CentoNIPT is a screening test – not a diagnostic test. This means, it can predict whether the risk of a genetic condition is high or low. The results will show whether any of the described chromosomal abnormalities have been detected in the fetus. However, CentoNIPT cannot diagnose a genetic condition with 100 percent certainty. A positive result indicates a substantial increased risk for a genetic abnormality. On the other hand, a negative result indicates a significantly decreased risk for the genetic abnormalities mentioned. If CentoNIPT is positive, the treating physician will usually offer you or the Patient an additional analysis to confirm the results and refer you for genetic counselling to discuss the implications and choices available for you and the fetus. Usually, invasive prenatal testing is recommended.

Limitations of CentoNIPT
- CentoNIPT detects the most common prenatal chromosomal abnormalities. However, CentoNIPT cannot rule out the possibility of other, less common genetic diseases.
- CentoNIPT is only designed to analyze full chromosome aneuploidies of the fetus after 10 weeks of gestation and is reporting on aneuploidies for chromosomes 21, 18, 13 and sex chromosomes (X0, XXX, XXY and XYY) in singleton and twin gestations.
- In case of organ transplantation from a male donor to the mother, sex chromosome status for the fetus cannot be determined.
- Because CentoNIPT analyzes both fetal and maternal cfDNA, there is a small chance that CentoNIPT may not reflect the chromosomes of the fetus but reflect chromosomal changes to the placenta (confined placental mosaicism), or in the mother (chromosomal mosaicism).
- Triple or higher gestations cannot be analyzed by CentoNIPT.
- In case of twin gestations and detection of only one Y chromosome by CentoNIPT, the fetal gender of each individual twin cannot be determined by CentoNIPT.
- Chromosome aneuploidies in general for a twin gestation can be detected by CentoNIPT but cannot be attributed to individual twin fetuses. In the case of uncertain or unambiguous results, the further analysis through invasive prenatal testing is usually recommended.
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- Negative results (reported as "**No Aneuploidy Detected**") do not eliminate the possibility of chromosomal abnormalities of the tested chromosomes. A negative result does not eliminate the possibility that the pregnancy has other chromosomal abnormalities (for example microdeletions), genetic conditions or birth defects.
- Results can be confounded by maternal and/or fetal factors like recent maternal blood transfusion, maternal weight, stem cell therapy and others.
- Please note that under the German Genetic Diagnostics Act the treating physician is only allowed to report the gender after the 12th week of the pregnancy.
- Due to legal restrictions - even if requested - fetal gender will not be included and/or disclosed in the report in selected countries (particularly China and India).

Potential Risks
CentoNIPT is considered non-invasive because it requires drawing blood only from the pregnant woman and does not pose any health risk to the fetus. Despite such, potential risks are: (1) If a blood sample is provided, there can be transient secondary bleeding and pain at the spot of the puncture and, rarely, local allergic reactions; the puncture can also result in bruising. However, these effects usually go away quickly. In very rare cases, the needle can damage a blood vessel or injure a nerve. Nevertheless, the spot of the puncture usually heals with no permanent effects. There are no further health risks associated with CentoNIPT. (2) The communication of the results of the NIPT may result in psychological stress for you or the Patient and family members. (3) If consent has been provided accordingly below, your or the Patient's genetic, and health data, including results of CentoNIPT may be shared with external doctors, scientific institutions, and/or (pharmaceutical) companies for their own scientific (including commercial) research, but solely in de-facto anonymized form. Nevertheless, the risk of re-identification of you or the Patient as a person cannot be completely excluded in theory, due to the uniqueness of genetic information. Such risk increases if and to the extent more information about you or the Patient is publicly available and can be linked to you or the Patient. Therefore, we recommend to handle such information with care, and not to publish in freely accessible databases or elsewhere on the Internet (e.g. for ancestry research), particularly not with any direct information or link to you or the Patient.

Data Protection Notice

CENTOGENE GmbH, Am Strande 7, 18055 Rostock, Germany ("**CENTOGENE**", "**we**" or "**us**") acts as the responsible controller for the collection, use, storage, or disclosure (hereinafter "**processing**") of your or the Patient's personal data. In this notice, "personal data" means any information relating to an identified or identifiable natural person. You can contact our data protection officer directly at the address above with the addition: Attn: Data Protection Officer, or by email at dataprivacy@centogene.com.

Data Processing
We collect a Sample containing biological material and certain personal data, including first name, last name, address, date of birth, gender, family relations, ethnicity, nationality, insurance information, participant code number (CGXXXXXXXX), disease, symptoms and other medical information, including image material, if provided (Art. 6 para. 1 a); Art. 9 para. 2 a) GDPR), which will then be processed in our databank. The Sample is analyzed using state-of-the-art scientific methods and the extracted data is processed with the collected data in our databank. then provide the results – containing genetic and health data of you or the Patient - to your treating physician. We archive the personal data and Sample for up to 10 years after the last result has been reported. We delete the data and destroy the sample thereafter, if has not already happened. Unless you consent otherwise as set out below, this data will be anonymized, which means that it will not be possible to reidentify you or the patient. However, the data may be of scientific importance when improving diagnosis and treatment of rare diseases, including scientific publications.

Data Storage
We archive the personal data and Sample for up to 10 years after the result has been reported. We delete or anonymize the personal data and destroy the biological material thereafter if this has not already happened. You or the Patient also have/has the option to process the personal data and donate the Sample for scientific (including commercial) research purposes. Then, personal data and Sample will be stored for up to 20 years after the last result has been reported. After 20 years at the latest, the Sample may be anonymized and stored in our archive in anonymized form for further scientific (including commercial) research purposes.

Recipients of Personal Data
In principle, we process personal data ourselves. Any transfer of personal data to a third party only takes place (1) with either explicit consent, (2) in order to fulfil a legal obligation or (3) if such transfer is permitted by law. In this regard, please be informed as follows:

- We use third party services, e.g. IT-service providers that maintain our systems or data centers which host such systems. Such third-party services are considered as data processors under GDPR. These data processors have been carefully selected, are contractually bound to comply with data protection laws, are subject to our instructions and regular monitoring and are only allowed to use the data they receive to fulfil their contractual obligations. We always agree on GDPR-compliant data processing agreements with such data processors.
- If consent has been provided accordingly below, we may provide biochemical, genetic and health data, including results of CentoNIPT – solely in de-facto anonymized form – to external physicians, scientific institutions and/or (pharmaceutical) companies for their own scientific (including commercial) research.
- We provide the results of CentoNIPT and the raw data to the treating physician and/or eventually to the requesting laboratory and may provide the results of CentoNIPT to the health care professionals who are involved in your or the Patient's medical counseling and/or clinical care.

International Data Transfer
The Sample will be analyzed in Germany. In principle, we process personal data solely within Germany, the European Union, and the European Economic Area, where GDPR-provisions apply. If the treating physician, and other recipients are located in a so-called third country outside the European Economic Area where GDPR provisions do not apply, your or the Patient's personal data shall be transferred to this third country. Such transfer will only take place with your or the Patient's consent. If a data processor is based outside the European Economic Area, we may transfer the personal data to such third country, subject to the further requirement that, either (1) the European Commission has decided that such third country already provides an adequate level of data protection or (2) we establish appropriate data protection safeguards with the data processor; e.g. by concluding so-called "standard contractual clauses" including — as the case maybe — supplemental clauses containing additional safeguards. In such cases, you or the Patient have/has a right to request a copy of these "standard contractual clauses". To do so, please contact our data protection officer.

Data Protection Rights Under the EU General Data Protection Regulation ("GDPR")

- Right to withdraw your consent with regard to data processing
- Right of access
- Right to data portability
- Right to rectification
- Right to erasure
- Right to restriction of processing
- **Right to object**
- Right to lodge a complaint with a supervisory authority

Additional Rights Under the German Genetic Diagnostics Act (Gendiagnostikgesetz)

- Right to withdraw your consent to CentoNIPT (until such has been performed)
- Right to request destruction of the Sample (as long as it has not yet been anonymized)
- Until the moment you or the Patient has been given the results of CentoNIPT, the right not to be informed about such results in full or in part (right not to know); and the right to request destruction of all such results

To exercise the rights, please contact our data protection officer.

Disclaimer
Please note that CentoNIPT is not definitive. Due to limitations in technology and/or incomplete medical knowledge, some disease-causing variants may not be detected. Therefore, it is not possible to completely exclude all risks for all possible genetic diseases. Moreover, in some cases, CentoNIPT may indicate a genetic abnormality when the fetus is actually unaffected (false positive) or may indicate no genetic abnormality when the fetus is actually affected (false negative).

IN CASE OF THE UNDERLYING CAUSE OF A FALSE-POSITIVE OR FALSE-NEGATIVE FINDING COULD NOT BE IDENTIFIED BY CENTOGENE, CENTOGENE SHALL NOT BE RESPONSIBLE FOR THE INCOMPLETE, POTENTIALLY MISLEADING OR INCORRECT RESULT OF CentoNIPT.

CentoNIPT® — Informed Consent Form

With my signature below, I confirm or confirm on behalf the Patient for whom I am the custodian or legal guardian (hereinafter, "**I**" or "**the Patient**") that I or the Patient have/has received, read and understood the preceding written explanation about the non-invasive prenatal testing. I or the Patient have/has been adequately informed regarding the purpose, scope, type and significance of such analysis, possible results and possible risks. The responsible physician has informed me or the Patient about possible prevention/treatment measures of any possible disease. Furthermore, I confirm that I have had sufficient opportunities to ask questions and such questions were answered in an understandable manner and to my or the Patient's full satisfaction.

Consent to the Non-Invasive Prenatal Testing and Related Data Processing

By signing this Informed Consent Form, I consent or consent on behalf the Patient for whom I am the custodian or legal guardian

(1) to non-invasive prenatal testing ("**CentoNIPT**") of my or the Patient's biological material ("**Sample**") by CENTOGENE GmbH, Am Strande 7, 18055 Rostock, Germany ("**CENTOGENE**") to screen for chromosomal abnormalities of the fetus as specified in the Information Sheet; (2) to any necessary processing of my or the Patient's personal data to perform such CentoNIPT as specified in the Information Sheet; (3) to provide the results of CentoNIPT to the treating physician and to be informed by the treating physician of the results of CentoNIPT; (4) to provide the results of the CentoNIPT to health care professionals who are involved in my or the Patient's medical counseling and/or clinical care, if so requested by the treating physician; (5) to provide the results of CentoNIPT to the requesting laboratory, as instructed by the treating physician; (6) to provide raw data of CentoNIPT, upon request, to the treating physician and/or the requesting laboratory; and (7) to store the personal data and the Sample for up to 10 years after CENTOGENE has reported the result and to anonymize the personal data.

Furthermore – if the following recipients are located in a so-called third country outside the European Economic Area, where GDPR provisions do not apply – I consent to the transfer of my or the Patient's personal data to this third country, in particular (1) to provide the results of CentoNIPT and the raw data to the treating physician and/or the requesting laboratory; and (2) to provide the results of CentoNIPT to the health care professionals who are involved in my or the Patient's medical counseling and/or clinical care. I acknowledge that such third country may not provide a level of data protection equivalent to the GDPR and may grant fewer or less enforceable data protection rights and no independent data protection supervisory authority to assist in exercising these rights.

Optional Consent to Further use of the Sample and Personal Data

I understand that the Patient's Sample and personal data may enable CENTOGENE to develop and improve diagnostic methods and therapeutic solutions for genetic diseases in general. This may help myself, my family members and other patients in the future. However, such voluntary consent is not necessary to conduct CentoNIPT as specified above.

I acknowledge that I or the Patient will not receive any compensation for the donation of the Sample and provision of personal data. I waive any claims for compensation, royalties, or other financial benefits that may arise from scientific (including commercial) research usage of the Sample and personal data.

(1) I consent to the usage of my or the Patient's Sample and personal data by CENTOGENE for scientific (including commercial) research, which focuses on the cause, early detection and/or treatment of rare diseases in general. I acknowledge that the Sample and data will be used in the interest of the greatest possible benefit to the general public for research which aims to improve the prevention, detection and treatment of rare diseases. Such includes but is not limited to disease areas such as metabolic disorders, neurodegenerative disorders, cardiac disorders and malformations as well as to diseases and genetic relationships that are still unknown today. As in any research on rare diseases – particularly due to the latest findings in genetic diagnostics – it is usually not possible to predict in detail which research questions and matters will be addressed in the future. Therefore, the specific research purpose cannot be detailed herein, and the Sample and data may also be used for medical research projects that cannot be foreseen today.

(2) I consent that CENTOGENE shares my or the Patient's biochemical, genetic, and health data, including results of CentoNIPT – solely in de-facto anonymized form – with external doctors, scientific institutions and/or (pharmaceutical) companies for their own scientific (including commercial) research. I acknowledge that "de-facto anonymized" means that the data available at CENTOGENE is altered in such a way, including redaction and removal of any pseudonyms, that re-identification of the Patient as a person for any further recipient of the data is practically impossible. However, the confidentiality risks described in the Information Sheet persist.

☐ YES

(3) I consent that CENTOGENE stores my or the Patient's Sample and personal data for 20 years after the last result has been reported and I hereby donate and transfer ownership of the Patient's Sample to CENTOGENE for further scientific (including commercial) research, which focuses on the cause, early detection and/or treatment of rare diseases in general. I acknowledge that after 20 years at the latest – once the identifying data was deleted – the Sample will become anonymized and will remain in CENTOGENE's archive – in anonymized form – for such scientific (including commercial) research. In anonymized form means, that CENTOGENE cannot identify the Patient as a person from such Sample anymore.

I understand that this consent is voluntary and is valid until such time as I choose to withdraw the consent. The consent with regard to (1) CentoNIPT can be withdrawn until such has been performed; and (2) to the processing of the personal data can be withdrawn at any time. Furthermore, the destruction of the Sample can be requested as long as it has not yet been anonymized; in each case with effect for the future.

Until the moment the results of CentoNIPT have been provided to me or the Patient, I understand I have the right (1) not to be informed about such results (so called right not to know); and (2) to request the destruction of all such results.

To withdraw the consent and/or to exercise the rights, I may contact CENTOGENE's data protection officer.

Date	Name and date of birth (DD.MM.YYYY) of the Patient	Signature of the Patient, and/or custodian/legal guardian
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Notice to the treating physician
The applicable law requires informed consent from the patient to be able to perform a non-invasive prenatal testing. Please ask your patient to sign the informed consent form. Alternatively, please confirm with your signature that the patient has consented accordingly and that you have such consent on file. Subsequently, please send the completed and signed informed consent form together with the information sheet and sample(s) to CENTOGENE.

Physician's Confirmation

I acknowledge that (1) the consent as shown above has been declared by the Patient and/or the Patient's custodian/legal guardian , (2) I have the Patient's and/or custodian's/legal guardian's signature on file if it is not shown above, (3) the Patient and/or custodian/legal guardian is capable of giving consent, (4) all questions of the Patient and/or custodian/legal guardian have been answered, (5) the Patient and/or custodian/legal guardian had the necessary time to consider the decision, and (6) the Patient and/or custodian/legal guardian until now have not exercised the right not to be informed of genetic testing results. I understand that (1) the Patient and/or custodian/legal guardian may exercise any of the rights specified in the Information Sheet and (2) I shall forward such requests to CENTOGENE without undue delay.

Date	Name of the treating physician	Signature of the treating physician
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