PATIENT CONSENT FORM

Panorama™ Prenatal Screen

SIGNED CONSENTS SHOULD BE KEPT IN THE PATIENT MEDICAL RECORD (do not return with the blood kit)

Purpose of the test

The Panorama™ Prenatal Screen is a non-invasive prenatal test used to screen the fetus for the chromosome abnormalities listed in the table below. You also have the option of requesting the reporting of fetal sex (where permitted by law). Panorama is performed on a maternal blood sample, which contains cell free DNA from both the mother and fetal placenta; the placental DNA is identical to the DNA found in the fetus in approximately 98% of pregnancies. Panorama is available for women who are at least 9 weeks pregnant. Your health care provider can provide you with more details about the chromosome abnormalities screened with this test.

Chromosome abnormalities evaluated with Panorama:	
Trisomy 21	This is caused by an extra copy of chromosome 21 and is also called Down syndrome. This is the most common genetic cause of intellectual disability and occurs in about 1 in every 830 live births[1]. Individuals with Down syndrome have an average IQ of 50 and all have some degree of intellectual disability. Some children with Down syndrome have defects of the heart or other organs that may require surgery or medical treatment. Some have other medical conditions including hearing or vision loss.
Trisomy 18	This is caused by an extra copy of chromosome 18 and is also called Edwards syndrome. Trisomy 18 occurs in about 1 in every 7500 live births and causes severe intellectual disability[1]. Some babies with Trisomy 18 have multiple severe birth defects of the brain, heart and other organs. Poor growth during pregnancy is common and many babies are miscarried or stillborn. Of those babies born alive, most die before one year of age. Babies who survive have profound intellectual disabilities and growth and development problems.
Trisomy 13	This is caused by an extra copy of chromosome 13 and is also called Patau syndrome. Trisomy 13 occurs in about 1 in every 22,700 live births and causes severe intellectual disability[1]. Most babies with trisomy 13 have multiple severe birth defects of the brain and other organs. Many babies are miscarried or stillborn. Of those babies born alive, most die before one year of age.
Monosomy X*	This is caused by a missing copy of the X chromosome and is also called Turner syndrome. This only affects girls and is found in every 1 in 5000 live births[1, 2]. Girls with Monosomy X are shorter than average. Some girls have heart or kidney defects, hearing problems, and some have minor learning disabilities. Girls with Monosomy X may benefit from growth hormone treatments in early childhood and usually need hormone replacement to enter puberty. As adults, they often have infertility.
Triploidy**	This is caused by an extra copy of all chromosomes. Abnormalities are often present in both the placenta and the fetus. It is found in about 1 in 1000 first trimester pregnancies[1]; most babies with triploidy are miscarried or stillborn. Of those rare babies born alive, most die before one year of age. Mothers carrying a baby with triploidy can also experience various pregnancy complications such as pre-eclampsia, severe nausea, excessive bleeding, and rarely persistent placental disease.

[1]*Nussbaum et al 2007 Thompson and Thompson Genetics in Medicine (7th Ed) Oxford Sounders, Philadelphia, PA;* [2]*Arthur Robinson & Mary G Linden, 1993, Clinical Genetics Handbook, Second Edition. Cambridge, Mass, Blackwell Scientific Publications*

* Monosomy X is not evaluated for dizygotic (non-identical) twin pregnancies or for pregnancies achieved using an egg donor or surrogate.

** Triploidy is not evaluated for twin pregnancies or for pregnancies achieved using an egg donor or surrogate,

Methods: Two tubes of blood are required from the mother. The samples are screened for only the chromosome abnormalities listed above. Incidental findings will **not** be reported.

- For singleton (one baby) pregnancies, the pregnancy will be screened for Trisomy 21, Trisomy 18, Trisomy 13, Monosomy X and Triploidy. Sex chromosome trisomies (XXY, XXX, and XYY) will also be reported, if identified.
- For twin (two baby) pregnancies, the pregnancy will be evaluated for zygosity. A zygosity test determines whether the twins are monozygotic (identical) or dizygotic (non-identical). Depending upon zygosity, different chromosome abnormalities will be screened.
    - Monozygotic (identical) twins will be screened for Trisomy 21, Trisomy 18, Trisomy 13, and Monosomy X. Sex chromosome trisomies (XXY, XXX, and XYY) will also be reported, if identified.
    - Dizygotic (non-identical) twins will be screened for Trisomy 21, Trisomy 18 and Trisomy 13 only.
- For singleton (one baby) pregnancies achieved using an egg donor or carried by a surrogate, the pregnancy will be screened for Trisomy 21, Trisomy 18, and Trisomy 13 only.

Test Results: Your test results will be sent to the healthcare provider who ordered the test.

- A 'low risk' result indicates a reduced chance that your fetus has the above listed chromosome abnormalities, but does not guarantee normal chromosomes or a healthy baby.
- A "high risk" result indicates that there is an increased likelihood your fetus has one of the chromosome abnormalities tested but does not confirm that the fetus has that abnormality. Prenatal diagnostic testing, such as chorionic villus sampling (CVS) or amniocentesis, or testing the baby after delivery, is recommended for confirmation, before any irreversible decision is made. Your healthcare provider will discuss recommended follow-up steps with you, which may include referral to a specialist.
- There is a chance that the sample(s) submitted will not return results or will return partial results; depending upon a variety of factors, a redraw may or may not be accepted. A repeat sample does not always return a result. Women who do not receive a

result from Panorama may be at unchanged or increased risk to be carrying a baby with a chromosome abnormality. If your Panorama test does not return a result, you should discuss options for further evaluation with your doctor, including the availability of genetic counseling, comprehensive ultrasound evaluation, and the option of diagnostic testing.

Panorama is not a diagnostic test – it will not confirm any of these chromosome abnormalities. It only determines whether you are at increased or decreased risk for these conditions in your current pregnancy. Therefore, **DECISIONS ABOUT YOUR PREGNANCY SHOULD NEVER BE MADE BASED ON THESE SCREENING RESULTS ALONE, AS THEY NEITHER CONFIRM OR RULE OUT THE PRESENCE OF A CHROMOSOME ABNORMALITY IN THE FETUS**. For definitive results, diagnostic testing should be performed during pregnancy or at birth to confirm or rule out a chromosome abnormality.

Test limitations and risks: Although this screening test will detect the majority of pregnancies in which the fetus has one of the above listed chromosomal abnormalities, it cannot detect 100% of pregnancies with these conditions. The results of this test do not eliminate the possibility of other abnormalities of the tested chromosomes, and it does not detect abnormalities of untested chromosomes, other genetic disorders, birth defects, or other complications in your fetus. Panorama was developed by Natera, Inc., a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA). This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA).

Inaccurate test results or a failure to obtain test results for one or more conditions may occur due to one or more of the following rare occurrences: courier/shipping delay; sample mix-up; laboratory failure or error; biological factors such as but not limited to: sample contamination or degradation, too little DNA from the fetus in the maternal blood sample, mosaicism (a mixture of cells with normal and abnormal chromosomes) in the fetus, placenta or mother, or other genetic variants in the mother or fetus; other circumstances beyond our control; or unforeseen problems that may arise. About 1 to 2% of all pregnancies have confined placental mosaicism – a situation in which the placenta has cells with a chromosome abnormality, while the fetus has normal chromosomes, or vice versa. This means that there is a chance that the chromosomes in the fetus may not match the chromosomes in the DNA screened from the placenta.

This test cannot be performed on patients who are carrying more than two babies (triplets or more), on patients who are carrying multiple babies (twin, triplets, etc.) where there is also an egg donor or surrogate, on pregnancies with a vanishing twin, or pregnancies in which the mother had a prior bone marrow/solid organ transplant.

Alternatives: Testing for chromosome abnormalities is optional. In addition to Panorama, there are other screening options available during pregnancy that can be discussed with your health care provider. If you want or need conclusive information about the fetal chromosomes, invasive diagnostic tests such as CVS or amniocentesis are available.

Confidential Reporting Practices: Natera complies with HIPAA confidentiality laws. Test results will be reported only to the ordering health care provider(s) or genetic counselor (where allowed). You may receive your test results directly 30 days after they are completed. Additionally, the test results could be released to those who, by law, may have access to such data.

Financial Responsibility: You are responsible for fees incurred with Natera for services performed. Once you have payed the asking price for the test at Spire – klinik for graviditetsscanning your financial responsibility has been fulfilled.

Genetic Counseling: If you have remaining questions about non-invasive prenatal testing after talking with your health care provider, we recommend that you make an appointment with a specialist who can provide more information about testing options.

PATIENT CONSENT FORM ADDENDUM
Five Microdeletion Panel
Panorama™ Prenatal Screen

Purpose of the Test

The purpose of the Panorama™ Prenatal Microdeletion Panel is to screen the fetus for the microdeletion syndromes listed in the table below. Your health care provider will determine if this test is appropriate for you and can provide you with more details about the microdeletion syndromes screened with this test. . **The Five Microdeletion Panel is only available for singleton (one baby) pregnancies where there is no egg donor or surrogate. It is not available for twins or pregnancies achieved with an egg donor or surrogate. For monozygotic twins only, 22q11.2 deletion may be ordered.**

Microdeletions Evaluated with Panorama Microdeletion Panel:

22q11.2 deletion syndrome (DiGeorge/Velocardiofacial syndrome)	22q11.2 deletion syndrome is usually caused by a small missing piece of chromosome 22. It is found in about 1 in 2000 newborns. Most children with this condition have mild-to-moderate intellectual disability and delayed speech and language. Many have heart defects, abnormalities involving the palate and/or immune system, and other health problems. Some people with this condition have autism spectrum disorder and some will develop psychiatric illnesses such as schizophrenia later in life.
1p36 deletion syndrome	This syndrome is caused by a small missing piece of chromosome 1 and is also called Monosomy 1p36. About 1 in every 5000 people has this condition. Children have moderate-to-severe intellectual disability. Most children have heart defects. Some children may need physical and occupational therapies to help with weak muscle tone. About half of children with Monosomy 1p36 have seizures and/or behavioral problems; some have hearing and/or vision loss.
Cri du chat syndrome (5p-)	This syndrome is caused by a small missing piece of chromosome 5 and is also called 5p minus (5p-) syndrome. About 1 in every 20,000 babies is born with this condition. Babies are usually small at birth with a small brain and head size. They often have breathing and feeding problems. Children with cri du chat have severe intellectual disability.
Angelman syndrome (15q11.2 deletion maternal)	Angelman syndrome (AS) is caused by a small missing piece of chromosome number 15, or from inheriting two copies of chromosome 15 from one parent and none from the other; there are other rare causes as well. About 1 in every 12,000 babies is born with this condition. Babies often have feeding difficulties and weak muscle tone. Children have severe intellectual disability and motor problems; most have a small brain and head size and some have seizures. Most children do not develop speech.
Prader-Willi syndrome (15q11.2 deletion paternal)	Prader-Willi syndrome (PWS) is caused by a small missing piece of chromosome number 15, or from inheriting two copies of chromosome 15 from one parent and none from the other; there are other rare causes as well. About 1 in every 10,000 babies is born with this condition. Babies have weak muscle tone and feeding problems. Children with PWS typically have intellectual disability, behavior problems, and delayed motor and language development. They also have excessive appetites and may become obese and develop diabetes.

(Gene Reviews: www.genereviews.org)

Methods: The additional microdeletion conditions listed above are performed in conjunction with the standard Panorama aneuploidy panel **only when requested** on the test requisition form. Samples are screened for only the chromosome abnormalities listed in the standard Panorama consent form and the microdeletion conditions listed above. Other incidental findings will **not** be reported.

Test Results: Your test results will be sent to the healthcare provider who ordered the test.

- A 'low risk' result for a microdeletion syndrome indicates a reduced chance that your fetus has a specific microdeletion, but cannot guarantee the fetus does not have a microdeletion syndrome.
- A "high risk" result indicates that there is an increased likelihood your fetus has a specific microdeletion syndrome, but does not confirm that the fetus has the condition. Prenatal diagnostic testing, such as chorionic villus sampling (CVS) or amniocentesis with a microarray is recommended for confirmation. Your healthcare provider will discuss recommended follow-up steps to you, which may include referral to a specialist and/or testing on one or both parents.
- There is a chance that the sample submitted will not return results for one or more of the microdeletion syndromes, even when results are received on the standard Panorama aneuploidy panel. Microdeletions of the maternally inherited chromosome are not detected below 6.5% fetal fraction for 22q11.2 deletion syndrome and 7% fetal fraction for the additional microdeletion syndromes.

Panorama is not a diagnostic test –it will not confirm the presence or absence of a microdeletion syndrome. Therefore, **DECISIONS ABOUT YOUR PREGNANCY SHOULD NEVER BE MADE BASED ON THESE SCREENING RESULTS ALONE, AS THEY NEITHER CONFIRM NOR RULE OUT THE PRESENCE OF MICRODELETION SYNDROME IN THE FETUS**. For definitive results, diagnostic testing should be performed during pregnancy or at birth to confirm or rule out a microdeletion syndrome.

Test limitations and risks: All risks and limitations outlined in the main Panorama consent form apply to the Panorama Microdeletion screening. See main Panorama consent form for details. In addition, the following limitations/risks apply:

- Panorama full microdeletion panel is NOT available for twin pregnancies or for pregnancies achieved using surrogate or egg donor.
- **If the mother is a known carrier for 22q11.2 deletion syndrome:** Panorama will not be able to return results on the fetus for 22q11.2 deletion syndrome. In this instance, it is recommended that you use another form of testing to detect the presence or absence of the 22q11.2 deletion in your fetus.
- **Risk of incidentally finding a maternal microdeletion:** This test screens for the 22q11.2 deletion in the fetus. However, it is possible during analysis that you may be identified to be at increased risk to be a carrier of a 22q11.2 deletion. If this occurs, the Panorama report will state that there is a 1 in 2 or 50% chance to have an affected pregnancy (as fetal status cannot be determined in this case). Because the Panorama test is not considered "diagnostic" for the mother of the fetus, your provider may offer additional testing to confirm if you carry the 22q11.2 deletion. In addition, finding out that you carry a microdeletion syndrome may cause feelings of anxiety or concern about your own health and well-being, as well as concerns about your pregnancy. Women who do not wish to risk finding out whether they carry this microdeletion should consider opting out of this screening test.
- If the percentage of fetal (placental) DNA in the sample is below 7%, screening for Angelman syndrome will not be performed and the results will be reported as "risk unchanged".

Alternatives to Panorama Prenatal Microdeletion Syndrome Screening: Maternal serum screening does not screen for microdeletion syndromes at this time. Other than the Panorama Microdeletion panel screen, you have the option of completing a diagnostic prenatal chromosome microarray on a CVS or amniocentesis sample. This will detect the above microdeletion syndromes, in addition to other microdeletions and microduplications that may be of clinical significance. You may also choose to have no prenatal screening or testing for microdeletion syndromes.

PATIENT CONSENT STATEMENT:

I have read or have had read to me the above consent addendum about the Panorama Prenatal Microdeletion Panel that is completed in conjunction with the Panorama Prenatal Screen when requested on the requisition form. I have discussed the reliability of test results and the level of certainty that a high risk test result for a certain disease serves as a predictor of such disease with my health care provider. I have had the opportunity to ask questions of my health care provider regarding this test, including the reliability of test results, the risks, and the alternatives prior to my informed consent. I request and authorize Natera to test my sample(s) for the above listed chromosome conditions and microdeletion syndromes. I understand that I must also sign this consent form, which will remain in my clinic chart.

I understand and hereby consent to the following processing activities with respect to the samples and related information I provide (Please check the applicable box(es) below):

☐ My samples and related information will be sent to a facility of Natera (as Data Processor) outside of the EU for performance of the test(s) ordered. (**Your consent is required in order for Data Processor to perform the ordered test(s).)**

☐ Data Processor may keep leftover samples and related information for future research & development, validation and quality assurance purposes, either independently or in collaboration with third-party partners; I and my heirs will not receive any payments, benefits, or rights to any resulting products or discoveries from the samples provided.

* If you do not consent to the use of your samples for future research & development, then your samples will be destroyed within 60 days after the performance of the ordered test. If you consent to the use of your leftover samples for future research & development, then leftover samples will be kept by Data Processor in compliance with applicable laws, including the GDPR.

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Signature of Patient Date

_____

Printed Name