Consent for the Luna Prenatal Test

A cell-based prenatal genetic test

Physician Name: _____ NPI number (required): _____

Instructions: to Provider
After obtaining the informed consent of the patient, please obtain her signature on the consent form and provide a signed copy to Luna Genetics. The signed consent form must be sent with the blood sample. If a signed consent is not submitted, Luna cannot perform the test. Electronic documentation of the patient's agreement is acceptable.

Terminology: a few unfamiliar words will be defined at the end of this document. Please make sure you understand them**.**

INTRODUCTION

The Luna Prenatal Test (a cell-based prenatal genetic test) is a new form of prenatal genetic testing developed by Luna Genetics. The clinical test was launched in April 2022. This consent form is intended to provide physicians, genetic counselors, and patients with information to help providers educate and patients decide whether the Luna Test is appropriate for a patient.

HOW THE TEST WORKS

Having the proper amount of genetic material (DNA) in each cell of the body is important for normal growth and development. The DNA is located along the 23 pairs of chromosomes (46 total) in each cell. This test is intended to detect chromosomal abnormalities including all forms of trisomy (an extra chromosome), monosomy (a missing chromosome), or missing or extra parts of a chromosome within a specific size range. Prenatal genetic tests are divided into noninvasive (a maternal blood draw) and invasive (meaning using a needle to obtain cells from the pregnancy by way of amniotic fluid or placental biopsy). Examples of invasive tests include chorionic villus sampling (CVS) and amniocentesis, which are associated with small risks of pregnancy loss. The Luna Test is a **noninvasive** maternal blood draw, which poses no risk of pregnancy loss.

Your provider can order the Luna Prenatal Test for you. If you decide to proceed with the test, 40mL (four 10mL tubes) of blood will be drawn from your arm and sent to the Luna Genetics laboratory. At Luna Genetics, the lab staff will test the blood to find rare fetal cells that are in your (maternal) blood. The Luna Prenatal Test works by recovering rare fetal cells in the mother's blood, called trophoblasts, which come from the placenta and contain fetal DNA. DNA is isolated from single trophoblasts, and many copies of the DNA are made, and then the DNA is sequenced using a method called Next Generation Sequencing. The number of copies of parts of the genome can be determined from the DNA sequence data. This allows for identification of extra or missing copies of entire chromosomes of parts of chromosomes. Missing copies of parts of chromosomes are called *deletions* and extra copies of parts of chromosomes are called *duplications*. The Luna Prenatal Test can detect all aneuploidy except triploidy (an extra copy of every chromosome) and most deletions or duplications that are associated with disease.

If the test result is abnormal, that means the fetus likely has a genetic abnormality such as an extra or missing whole chromosome or part of a chromosome and will be identified in the report. A specific genetic abnormality may be associated with health problems which will be explained to you by your provider in the event of an abnormal result. In the case of an abnormal result, it is important to be as certain as possible about the finding. Your provider(s) (physician and/or genetic counselor) will review all information obtained in the current pregnancy, including any other genetic test results and ultrasound findings, to inform you of the degree of certainty that the fetus has the specific abnormality or not. This may involve additional testing or additional consultations and/or genetic counseling. Various professional organizations recommend that a diagnosis (particularly for trisomy or sex chromosome aneuploidy) should not be based on analysis of DNA from trophoblasts alone, so if your test result is abnormal, it is likely that your provider will recommend some combination of ultrasound, CVS, or amniocentesis before drawing a definite conclusion that the fetus is affected by a trisomy or sex chromosome aneuploidy.

If the test result is normal, that means that none of the abnormalities analyzed by this test were found to be present. A normal result does not guarantee that the pregnancy is completely healthy.

See "Potential Risks" below for discussion of false positive or false negative results. For any genetic test result, there is a small possibility of a false positive or a false negative result which means the test result is incorrect. The chance of an incorrect result from the Luna Prenatal Test is quite low.

LIMITATIONS OF THE TEST

The test does not distinguish whether a trisomy is free-standing or is associated with a translocation. The test cannot reliably detect chromosomal deletions smaller than 1.5 Mb, duplications smaller than 2 Mb, triploidy (an extra copy of every chromosome), or uniparental disomy (an abnormality in which two copies of a chromosome come from one parent as compared to the normal one copy from each parent). The test will usually detect inherited unbalanced translocations but does not distinguish a balanced translocation result from a normal result. The test is not designed to detect single gene conditions such as cystic fibrosis, sickle cell anemia, Rett syndrome, fragile-X syndrome, and hundreds of others. No test, including the Luna Prenatal Test, guarantees the birth of a genetically normal child.

PLACENTAL MOSAICISM

Placental mosaicism means that there is more than one type of cell in the placenta, (usually some cells with an extra or missing chromosome and some cells with normal chromosomes). This occurs in about 2% of CVS and Luna Prenatal Test cases; thus, mosaicism is NOT present in 98% of cases. If mosaicism is detected, your provider will explain the significance and provide you with options for further testing (sometimes, amniocentesis).

TWINS

Luna is not accepting samples from twin pregnancies or higher multiple pregnancies at this time.

WHAT THE LUNA TEST DETECTS

Based on validation studies available in the form of a white paper on its website (www.lunagenetics.com), Luna Genetics has demonstrated that the Luna Prenatal Test is highly reliable for detection of all trisomies and monosomies including trisomy 13, 18, and 21 and sex

(X and Y) chromosome aneuploidies. The test is designed to detect nearly all the conditions known as chromosomal disorders. Luna's data indicate that the test is reliable for detection of deletions (missing pieces of chromosomes) down to a size of 1.5 Mb (megabase or one and a half million DNA letters) and for detection of duplications (extra pieces of chromosomes) down to a size of 2.0 Mb. Some cells are in the process of copying their DNA (in S phase of the cell cycle). These cells are not useful for detecting small deletions or duplications. These cells are reported for "aneuploidy only." Most cells are scored for "aneuploidy + 1.5/2.0 Mb del/dup."

DETAILS OF CONCEPTION AND THE PREGNANCY

The Luna Prenatal Test is reliable for detection of fetal chromosomal abnormalities in cases of IVF including those arising with an egg donor. However, it is essential that the patient and provider supply certain information to the laboratory for the most accurate testing. This information should include maternal age, gestational age by last menstrual period (LMP) or ultrasound dating, any use of fertility drugs with or without other assisted reproductive technology (intrauterine insemination, IVF, etc.), the use of donor egg or sperm, and if there have been any abnormal test results in the pregnancy (i.e. abnormal NIPT or US finding). In the case of IVF, include the number of embryos implanted and the results of any preimplantation genetic testing for aneuploidy (PGT-A). The provider must provide this information on the requisition form.

POTENTIAL BENEFITS OF THE LUNA PRENATAL TEST

Since the Luna Prenatal Test is a maternal blood test, there is no risk to the fetus. The Luna Prenatal Test offers for the first time the ability to detect most copy number abnormalities that would be detected by CVS or amniocentesis using a risk-free maternal blood sample. Validation studies were performed as described in a white paper on the Luna website. The Luna Prenatal Test has optimal performance from 9 to 14 weeks of gestation but can be performed as early as 8 weeks and is reliable through 22 weeks. Before and after 9-14 weeks, the test is still reliable, but there is an increased risk of not finding enough fetal cells in the maternal blood. Current validation and performance data are available at www.lunagenetics.com and will be updated at intervals.

POTENTIAL RISKS INCLUDING FAILURE TO CAPTURE TROPHOBLAST CELLS

The most frequent difficulty with the Luna Prenatal Test is the failure to recover fetal cells in the mother's blood sample. If during the first day or two of the test procedure Luna Genetics is unable to recover enough fetal cells in the blood sample, you will be encouraged to undergo a second blood draw promptly (at no extra lab cost to you). This occurs ~10% of the time. Overall, reportable results are obtained 90-95% of the time after analyzing a blood redraw when offered. If no cells are reported, all laboratory charges will be **refunded**, and there would usually still be time for you to obtain an amniocentesis and possibly CVS. The full Luna Prenatal Test evaluates for both aneuploidy and deletions/duplications down to a size of 1.5 Mb/2.0Mb, respectively. In cases where results are reported for aneuploidy only, unlimited redraws will be processed at no additional cost.

False positive or false negative results with the Luna Prenatal Test are expected to be quite rare and potentially similar to the rates for CVS and amniocentesis. More precise information as to the frequency of false positive or false negative results will not be known until more tests are performed. A false negative test result is possible for small deletions. The risk of detecting placental mosaicism is about 2%, which is similar to the risk with CVS

testing. There are many very rare possibilities that can occur when performing genetic testing, and no form of genetic testing is expected to be perfect.

What is the sensitivity, and specificity, positive predictive value, and negative predictive value for the Luna Prenatal Test?

As stated above, there is a risk that no usable cells will be recovered for a singleton pregnancy. Luna treats these cases as failed tests. When calculations are based on successful tests where data were available from CVS or amniocentesis and from the Luna Prenatal Test, the sensitivity was 100% (95% CI 54.1% - 100%). The specificity was 100% (95% CI 91.8% - 100%). The positive predicative value was 100% and the negative predictive value was 100%. It is expected that there will be rare instances related to placental mosaicism where the Luna Prenatal Test correctly detects aneuploidy in trophoblasts, but this abnormality will not be present in CVS mesenchymal core (cultured CVS) or amniocytes (amniocentesis). This defines confined placental mosaicism. These current data are based on **a sample of 49 fetuses in 48 pregnancies**, and some confidence limits are quite wide. Luna is currently expanding the data set, and these numbers will be updated on the website. There were 6 singleton pregnancies for which no cells were recovered, and these cases are omitted from the calculations. Please see White Paper for details.

POTENTIAL FOR LEARNING GENETIC INFORMATION ABOUT FAMILY MEMBERS

Luna Genetics may discover a harmful deletion in the pregnancy that may be inherited from a parent or be new in the current pregnancy. In such cases the mother's DNA will not be analyzed, but providers can refer to other laboratories for testing. If a deletion is of uncertain significance, your (maternal) DNA may be tested to determine if the finding is inherited from you. If no DNA sample is collected from the father, as is usually the case for the Luna Prenatal Test, there is no potential to identify non-paternity.

OTHER TESTING

There are multiple alternative forms of prenatal genetic testing including maternal serum screening, first trimester combined screening, ultrasound studies including nuchal (neck area) translucency, CVS, amniocentesis, and cell-free NIPT. Alternative forms of testing should be discussed with your healthcare provider.

CONFIDENTIALITY

Luna complies with HIPAA confidentiality laws. Test results will be reported only to the ordering health care provider(s) or genetic counselor (where allowed). You must contact your provider to obtain the results of the test.

GENETIC COUNSELING AND PHYSICIAN REFERRAL

New York state requires that genetic counseling be offered prior to signing this consent and should be available after the test. Further testing or additional physician consultation may be warranted.

COST AND POTENTIAL FOR INSURANCE REIMBURSEMENT

Because there is not yet any experience with obtaining insurance coverage for the Luna Prenatal Test, Luna requires advance payment in full before performing the test. Luna anticipates that insurance companies may approve payment and provide reimbursement to you, especially if the Luna Prenatal Test substitutes for genetic testing that might otherwise have

been performed, such as CVS or amniocentesis. Information for insurance providers will be available at lunagenetics.com including a policy statement and other information that can be submitted to your insurer.

DISPOSITION OR RETENTION AND RESEARCH USE OF SAMPLES.
Signing this consent allows Luna to use residual cells or DNA to try to improve the Luna Prenatal Test or for other research intended to improve reproductive health care. You may decline to allow this use of the cells or DNA by checking the box below.

☐ I choose to opt out from future use of residual cells or DNA from my blood sample. If you check this box, all residual tissue will be destroyed 60 days after the presumed delivery date for this pregnancy.

CONSENT

Your signature below indicates that you have read this consent form, that you have had the opportunity to ask your obstetrician or genetic counselor questions that you have, and that you understand the risks and benefits of Luna Prenatal Testing.

☐ If you check this box, you also authorize the ordering provider to share other genetic information with Luna Genetics about your pregnancy such as family history, any abnormal screening or diagnostic test results already obtained in the current pregnancy, and any other information that the provider believes will help the performance of the Luna Prenatal Test. Much of this information is requested on the requisition form, but this consent relates to information that is available after the Luna blood draw. This information will be treated as HIPPA protected sensitive patient health information.

Patient name: _____ Date of birth: _____

_____ Date of consent: _____
Signature of Patient

Person obtaining consent:

Name of person obtaining consent: _____

Signature of the person obtaining consent: _____

Date consent obtained: _____

Terminology

- **Aneuploidy:** an extra or missing chromosome, includes trisomy and monosomy
- **Deletion:** a missing segment of DNA in a chromosome
- **Duplication:** an extra segment of DNA in a chromosome
- **Megabase (Mb)**: a DNA length of one million bases or letters
- **Monosomy:** a missing chromosome, e.g., monosomy 21
- **Mosaicism:** more than one cell type, usually some cells with normal chromosomes and some with abnormal chromosomes
- **NIPT, cell-free NIPT:** noninvasive prenatal testing, the current test that is widely used
- **Preimplantation Genetic Testing-Aneuploidy (PGT-A):** A form of genetic testing often performed on embryos prior to implantation as part of the IVF process
- **Singleton:** a single fetus rather than twins or other multiples
- **Triploidy:** an extra copy of all chromosomes
- **Trisomy:** an extra chromosome, e.g., trisomy 21
- **Uniparental disomy:** an abnormality in which two copies of a chromosome come from one parent and no copy from the other parent, as compared to one normal copy from each parent