Patient informed consent

neoBona® is a non-invasive prenatal screening that analyses cell-free fetal (placental) DNA in the mother's blood by whole-genome sequencing to estimate the risk of specific chromosomal abnormalities in the fetus. Genetic counselling by a medical doctor or a specialized genetic counsellor is recommended to explain the test, the result, and the possible implications.

All **neoBona®** options are carried out entirely at SYNLAB laboratory in Spain, being performed by “massively parallel DNA sequencing” with paired-end reads and determines the fetal fraction.

neoBona® determines the risk of trisomy 21, trisomy 18 and trisomy 13 in the fetus and, if specifically requested, it evaluates the X and Y chromosomes providing information on the fetus sex and possible aneuploidies of the sex chromosomes (X0, XXX, XXY and XYY). "Trisomy" is the term used to describe the abnormal presence of three, instead of the expected two copies of a particular chromosome:

- Trisomy 21 is due to an additional copy of chromosome 21. This trisomy causes Down syndrome, which is diagnosed in approximately one in 750 newborns. Children with Down syndrome may have mild to moderate intellectual impairment, heart defects and other disorders.
- Trisomy 18 is due to an additional copy of chromosome 18. This trisomy causes Edwards syndrome, which occurs in approximately one in 7,000 newborns. The majority of affected pregnancies end in spontaneous miscarriage. Edwards syndrome is characterized by severe mental retardation and a large range of malformations; the majority of affected infants die during the first year.
- Trisomy 13 is due to an additional copy of chromosome 13. This trisomy causes Patau syndrome. Infants with Patau syndrome have severe mental retardation, can exhibit severe congenital heart malformations as well as other pathologies, and rarely survive beyond 1 year of age. It is estimated that one in 15,000 newborn babies has Patau syndrome.
- Aneuploidies of the sex chromosomes (X, Y) are most commonly associated with Turner's syndrome and Klinefelter's syndrome. The external appearance of these syndromes is significantly milder than in the trisomies described above. In most cases, these come up in the investigation of the causes of infertility problems. Aneuploidies of the sex chromosomes can only be examined in singleton pregnancies.

To be eligible for any of the options person must be at or beyond 10 weeks of gestation (10w + 0d), with a single or twin pregnancy (1 or 2 fetuses) resulting from natural conception or from in vitro fertilization (IVF), including pregnancies after gamete donation. Persons with more than two fetuses are not eligible. The test can be used in vanishing twin or fetal reduction pregnancies, although in these situations there may be an increased risk of a false positive or false negative result. Your medical specialist must determine which test is the most appropriate for you.

neoBona® is a screening test and is not intended nor validated for diagnostic testing; it has certain limitations, including false negative and false positive results. Fetuses with normal euploid chromosome numbers (non-trisomic) may occasionally be classified as “consistent with presence of trisomy” (false positive result). A test result “consistent with presence of trisomy” and/or other indicators suggestive of a chromosomal abnormality should always be confirmed by invasive prenatal test (e.g. amniocentesis), before making any irreversible clinical decision.

This screening test only analyzes specific chromosomal abnormalities so not all abnormalities will be detected; on rare occasions, a fetus with aneuploidy can be classified as "consistent with no aneuploidy" (false negative). A normal result does not discard the possibility that the fetus may have chromosomal, genetic, or congenital abnormalities (e.g., open neural tube defect), nor does it assure a healthy fetus.

There is a possibility the results do not reflect the fetus chromosomes due to fetal and / or maternal factors such as confined placental mosaicism (CPM), maternal mosaicism, maternal neoplasia (benign or malignant) or recent blood transfusion, among others. CPM may be associated with an increased likelihood of complications during pregnancy or uniparental disomy (UPD), which can affect the growth and development of the fetus.

No irreversible clinical decisions should be made based solely on **neoBona®** test results; results should be always interpreted in the light of other clinical findings, and it is recommended that the results are told to the person by a health-care professional in a suitably adapted consultation. Genetic counselling is recommended.