The undersigned Mrs._____Born in _____the_____and

Ms._____borne in _____the _____

Being _____ _____

Declare

-having discussed with Dr_____in the context of genetic counseling, the characteristics, potentials and limitations of prenatal examination based on the microarray
-to have had the opportunity to ask all questions considered appropriate,
-to have received comprehensive and understandable answers,
-and to consider all the information received (and contained in the INFORMATION FOR THE SURVEY USING CHROMOSOMIC MICROARRAYS IN THE PRENATAL TIME attached to this consent form) appropriate and exhaustive.

Therefore, based on the information received

☐ *Consent* ☐ *Do not consent*
to the execution of the CGH array test on fetal DNA, to the withdrawal of their peripheral blood sample and to the possible extension of the CGH array analysis to themselves using the aforementioned sample-

The undersigned also declares / declare that they wish to receive information:

☐ on all variants / CNV highlighted
☐ only on variants /CNV with clear pathogenic significance related to the indication for analisis
☐ For all variants /CNV with clear pathogenic significant regardless of the indication for the analisis
☐ _____

The undersigned also declare/declares to:

Want DO NOT want the biological material to be used anonymously for studies or research.

Want DO NOT want the biological material collected to be kept until the end of the diagnostic process and that the biological materials and the resulting reports can be used for studies and research aimed at protecting the community in the medical, biomedical and epidemiological fields, with particular reference to programs for the verification of the quality of the performance of the clinical analysis laboratories, guaranteeing the anonymity of the patient

Want Do NOT want to share the results with Dr. _____

The undersigned declare that the above is true and undertake to promptly communicate any change of opinion on the matter.

Signature_____Signature_____

Signature_____Signature_____

Healthcare personnel who have access to personal data abide by the rules of the Privacy Law: ***General Data Protection Regulation of the European Union 2016/679 (GDPR)***

Signature and stamp of the specialist who collected the informed consent

_____ Date_____

I also declare that I am aware of the possibility to **REVOKE** this consent at any time by written communication to the competent structure

*The undersigned*_____*on date* _____

Declare of wanting to REVOKE the consent communicated above

Signature _____

INFORMATION FOR THE INVESTIGATION USING CHROMOSOMAL MICROARRAYS IN THE PRENATAL PERIOD

What is the analysis with chromosomal microarray?
What can be detected with chromosomal microarrays?
The analysis with chromosomal microarray (CMA; Chromosome Microarray Analysis) is a technique capable of simultaneously analyzing all chromosomes in greater depth than the standard fetal karyotype: it allows to identify very small chromosomal alterations, which cannot be highlighted with the analysis of classical fetal karyotype.
The method, however, as better explained below, has limits and problems of interpretation for which its use must be carefully evaluated, especially in the prenatal period.

What are the indications to the CMA?
Before birth, the most appropriate and frequent indications for the use of this method of investigation are:
- the need to characterize in more detail some fetal chromosomal anomalies;
- the finding on ultrasound of structural abnormalities of the fetus;
- a fetal underdevelopment with early onset of uncertain cause.

What are the limits of this diagnostic method?
Like any diagnostic method, CMA also has limitations. In particular, the following are generally not evident:
1. balanced chromosomal rearrangements (e.g. reciprocal translocations, inversions);
2. poorly represented chromosomal mosaicism (<30%);
3. chromosomal variants / anomalies not detectable with the microarray platform used;
4. genetic pathologies not caused by chromosomal duplications / deletions.

Any maternal contamination (simultaneous presence in the sample of fetal and mother cells) can affect the reliability of the result: in some cases it is advisable to exclude any contamination of the fetal sample with maternal cells. This investigation requires the comparison of fetal DNA with maternal DNA.
The presence of imbalances may make it necessary to use additional techniques to characterize the rearrangement and may make it necessary to extend the analysis to both parents in order to correctly interpret the result.
For these reasons, the fetal sample should always be accompanied by a blood sample from the parents, which is used only in cases where it is necessary to make a comparison between the fetal profile and the parental one. In these cases, more time is usually required for diagnostic conclusions.
In rare cases, the results of the examination could reveal the biological mismatch between the couple's DNA and the fetal one (for example in the case of heterologous fertilization). Incorrect information on the biological role of the couple could prevent a correct interpretation of the test.

Are the results provided by the method always easy to interpret?
The analysis of the results can sometimes be problematic, since the study of the genome using chromosomal microarrays may result in variants (technically called Variations in the Number of Copies; CNV) that are not easy / immediate to interpret, such as:

- rare variants / CNVs, for which there aren't still sufficient knowledge to understand whether they are benign or potentially associated with diseases of some kind. These variants are called VOUS (variants of uncertain meaning);

- variants / CNV with pathogenic significance, but for which the existence of a link with the condition for which the analysis was indicated is not certain;
- variants / CNV associated with pathologies with variable expressivity and incomplete penetrance (for which the disease possibly associated with the highlighted rearrangement may not manifest itself or manifest itself with variable and unpredictable severity) or susceptibility to complex diseases;
- variant / CNV variants that have clinical implications not correlated with the indication to the analysis (e.g. pathologies with late onset, predisposition to the onset of tumors, healthy carrier status of recessively transmitted diseases, etc.), occasionally with family transmission.

What are the main technical characteristics of the method that will be used?

Appropriate use of CMA (Chromosomal Microarray Analysis) techniques in prenatal diagnosis
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In order to reduce the possibility of identifying variants of uncertain significance, the test will be carried out using filters that mainly search for imbalances of regions responsible for microdeletion / microduplication syndromes and / or containing disease-genes: in these 'critical' regions the resolution is about 100-200 Kb; all other regions of the genome will still be analyzed, but with a 500 kb filter.

When will the test result be available?
Within about 10 days of DNA extraction from fetal cells (cell culture, chorionic villous frustules, amniocytes) the test result will be available and will be delivered to the parents during a genetic consultation.
In particular cases, however, extensions of the time necessary to provide a response are possible.