NIMGenetics
New Integrated Medical Genetics

COD.

To be filled by the laboratory

INFORMED CONSENT

TrisoNIM® Advance ◯	TrisoNIM® Premium ◯	TrisoNIM® Excellence ◯	TrisoNIM® Twins ◯

PATIENT AND SAMPLE DATA

Indentification code	
Date of sample extraction	
Name and Surname	
ID	Telephone number
E-mail address	
Address	
Postal code	City

CLINICAL DATA

Date of birth	
No of fetuses	◯ Vanishing twin
Weeks of gestation	

Reason for consultation

- ◯ No relevant comments
- ◯ Increased Nuchal Translucency
  Specify _____
- ◯ Ultrasound Markers
  Specify _____
- ◯ Risk in combined screening
  Specify _____
- ◯ Other (family history, affected children, etc.)
  Specify _____

MEDICAL PRACTITIONER DATA

Name	Telephone number
Clinic / Hospital / Laboratory	E-mail address

1. I have received information on the indication, purpose, characteristics, scope and limitations of **TrisoNIM®**, and I have had the opportunity to read the information provided about the test through the information sheet attached to this document, and my questions have been answered satisfactorily.
2. I understand that **TrisoNIM®** is a screening and not a diagnostic test.
3. I understand that, despite the high sensitivity of the test, a low-risk result does not exclude the possibility of foetal chromosomal disorders.
4. I understand that a high-risk result must be confirmed by an invasive prenatal diagnostic test.
5. I understand the limitations of this test described in the attached information sheet and confirm that I have informed my physician of circumstances that may affect the reliability of the test, should any of them occur.
6. I understand that the results of this test do not replace the medical diagnosis made within a medical visit, nor the genetic counselling given by your doctor, recommending that these results be shared in a medical visit, where, in addition, the genetic counselling described in the attached information sheet should be carried out. **NIM**Genetics, S.L. shall not be liable for any use made by you or your doctor of the results obtained, nor for any harmful consequences that may derive from the use of such information.
7. I want to know the sex of the foetus: **YES** ◯ **NO** ◯
8. I understand that, by performing this test, genetic information not related to the medical concern for which this test has been requested may be obtained on the foetus or the mother. These findings, which would be included as an informational note in the report of results, may require additional testing. I check this box to indicate that I **DO NOT WANT** this information to be disclosed to me. ○
9. I understand that the information obtained may also have implications for other family members, as well as the desirability of transmitting such information to them myself in this case.

For all the reasons above, I declare the aforementioned to be true and accurate and I give my consent to carry out the **TrisoNIM®** test in the contracted modality.

Signature Patient/Legal Guardian _____ **Signature Medical Practitioner** _____

Date _____

◯ I consent to the use of my anonymous clinical information and the results obtained for scientific publications, quality studies, and databases in the health field, maintaining strict confidentiality about my identity.

◯ I consent to the transfer of my anonymised data to third parties for use in the field of scientific research. Data anonymization means that they will be subject to a process whereby it is no longer possible to reasonably establish the link between the information obtained from the analysis carried out and your identity.

◯ I authorise **NIM**Genetics, or its affiliates, to send me information related to its products and services.

Signature Patient/Legal Guardian _____ **Date** _____

NIMGenetics S.L. - Parque científico de Madrid - C/Faraday, 7 (Campus de Cantoblanco) 28049 Madrid - CIF B-85332138

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General Information About TrisoNIM®: Purpose And Risks

In accordance with the provisions of Law 14/2007, of 3 July, on Biomedical Research, it is hereby informed that TrisoNIM® is a prenatal screening test that is carried out by analysing the foetal DNA present in maternal blood, through which the risk of the foetus carrying certain chromosomal abnormalities is assessed.

NIMGenetics currently performs four TrisoNIM® prenatal screening test options: Advance, Premium, Excellence, and Twin. In its four options available, this test assesses the risk of foetal trisomy for chromosomes 21 (Down Syndrome), 18 (Edwards Syndrome) or 13 (Patau Syndrome) with a detection accuracy of approximately 99% for these trisomies, as well as the risk that the foetus may carry alterations in the sex chromosomes. This analysis of the X and Y sex chromosomes will also make it possible to know the sex of the foetus, if you so wish.

In the case of the Advance option, this study also assesses the risk of microdeletion syndromes 1p36, 2q33.1 or 5p15 (Cri-du-Chat Syndrome).

In addition, the Premium option, the risk of microdeletion syndromes 10p14-13, 11q23-qter (Jacobsen Syndrome) or 16p12-p11 and trisomies 9, 16 or 22 is also assessed.

In addition to the above categories, the Excellence option also assesses the risk of microdeletion syndromes, 1p32p31, 2p12p11.2, 2q33.1, 3pter-p25, 4p16.3, 4q21, 5q12, 5q14.3q15, 6pterp24, 6q11q14, 6q24q25, 8q24.11-q24.13 (Langer-Giedion Syndrome), 9p, 10q26, 11p11.2, 11p13p12 (WAGRO and WAGR syndromes), 14q11-22, 14q22 (including Frias Syndrome), 15q26qter (Congenital diaphragmatic hernia type I and Drayer Syndrome), 15q11-q13 (Angelman and Prader Willi syndromes), 16q22, 17p13-p11.2 (Yuan-Harel-Lupski, Miller-Dieker, and Smith-Magenis syndromes), 18q, 18p, and 22q11.2 (Digeorge Syndrome), and the microduplication syndromes in 15q11-q13, 17p11.2, and 17p13.3.

Finally, the Twin option can detect chromosomal aneuploidies, but these cannot be traced to individual foetuses. If a Y chromosome is detected, the test cannot determine the foetal sex of each twin. In these cases, the presence of microdeletions or alterations in the sex chromosomes will not be reported.

In the event that one of the foetuses is lost (vanishing twin), the pregnancy will continue to be considered, as far as foetal DNA is concerned, as a twin pregnancy.

TrisoNIM® can be performed as early as the 10th week of pregnancy and does not pose any risk to the foetus, as only 10 ml of maternal blood needs to be collected. The blood will be drawn by venepuncture, which may involve a series of risks, usually minor and infrequent, among which bleeding may be highlighted.

Location Where the Analysis will be Carried Out and Use of the Biological Sample at the End of the Analysis

This test will be carried out by NIMGenetics technical staff at the laboratory owned by this company, which is located in Madrid.

The remaining samples will be stored encoded for a maximum period of 3 months, to be used in those cases where the study needs to be repeated for diagnostic confirmation, given that they are only suitable for carrying out prenatal screening but not for carrying out additional or confirmatory diagnostic tests, which must be carried out on foetal samples. The material generated from the DNA obtained from the samples, called *genomic libraries*, will also be stored encoded for a period of 1 year, to ensure its preservation until the end of the gestation period.

Only authorised NIMGenetics personnel will have access to the connection between your biological sample, your DNA and the information obtained by processing it, and the code assigned in each case.

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Test Results

TrisoNIM® is a screening test, not a diagnostic test, although it is very accurate to identify foetal chromosomal abnormalities (with a detection accuracy of approximately 99% for trisomies 21, 18, and 13). However, the implications of the potential results must be considered before carrying out the test.

- Implications of a positive result:

  False positives have occurred, therefore, if a high-risk result is obtained, the alteration must be confirmed by an invasive prenatal diagnostic test (amniocentesis or chorionic villus biopsy). In some cases, this will have to be associated with specific studies on the parents.

- Implications of a negative result:

  Although this test has a high sensitivity to detect alterations, a low-risk/non-detection result does not entirely exclude the possibility of a foetal chromosomal abnormality.

- Implications of a non-informative result:

  In some cases (less than 0.1% of the studies carried out), it will not be possible to obtain a clear result because the blood sample does not contain enough foetal DNA, due to various clinical reasons such as early gestational age or high maternal weight, among others. It may be necessary to take a new blood sample in these cases so that the test can be repeated, or to resort to invasive prenatal diagnostic tests.

The report will be available in less than 7 working days in average, to be counted as of the moment the laboratory receives the sample. In rare cases (less than 1%), this period may be extended due to various methodological causes. The turnaround times for each test option can be checked at www.nimgenetics.com

Limitations of the Test

The following situations make it impossible to obtain a reliable test result:

- Genetic changes in the placenta (confined placental mosaicism) or in the mother (in the presence or not of chromosomal mosaicism) mean that test results may not reflect genetic changes in the foetus.
- A limited number of foetal cells carry one of the genomic alterations analysed (foetal mosaicism).
- Chromosomal alteration in unanalysed regions.
- Complete triploidies or chromosome microdeletions in the regions analysed with a size below the resolution limit of the technique, which is currently considered to be approximately 10Mb.
- Blood transfusions, transplants, immune therapy, or stem cell therapy prior to blood sampling.
- Gestational age earlier than the 10th week or later than the 25th week.
- Triplets or pregnancies with a higher number of foetuses.

The no-information rate may be increased in morbidly obese patients or in patients being treated with low molecular weight heparin.

You are responsible for informing your doctor about any of these circumstances.

Likewise, the technology used will not make it possible to detect other genetic alterations such as rearrangements, changes in the sequence, repetitive expansions of trinucleotides or epigenetic alterations, which could cause the same or similar pathologies to those secondary to some microdeletions or microduplications included in this test.

Incidental Findings

The **TrisoNIM®** test analyses other regions of the genome not included in the specified chromosomes and microdeletions. It is important to understand that, on exceptional cases, we can identify genetic alterations in the foetus or mother in these regions. This incidental finding will be included in the report of results as an informative note, if you give your consent, because the analysis of these regions cannot be carried out with the same statistical accuracy as the genetic regions that are the subject of this study. These findings may require additional invasive or imaging tests. You must decide whether or not you wish to receive this additional information by completing the appropriate section at the beginning of the document.

In addition, the information obtained may also have implications for other family members and, in this case, it is advisable that you share this information with them so that, if they wish, they can make arrangements for a genetic consultation where they will be informed about their personal risk and their future healthcare options.

Genetic Counselling

The medical practitioner who requests/advises this test undertakes to provide information about the purpose of the analysis and provide genetic advice once the analysis results have been obtained and evaluated. NIMGenetics is available to this professional to clarify any questions that may arise.

Data Protection and Confidentiality

Personal data and the genetic test results can only be accessed by duly authorised NIMGenetics technical and health personnel. This information will be confidential and shall be processed in accordance with the European Data Protection Regulation (Regulation (EU) 2016/679). The personal data that you provide us with, as well as those obtained from the analyses carried out, will be included and registered within the information processing systems of NIMGenetics for the diagnostic purpose described throughout this document. If you are not satisfied with the aforementioned processing, we will be unable to carry out the requested analysis. Likewise, we inform you that your personal information will not be disclosed to any person outside NIMGenetics, except for those who you authorise as requested in the following section "Further use of data", or as required by law. However, your personal information will not be used for any purpose other than that reported here, or that is incompatible with it.

In compliance with Law 14/2007, of 3 July, on Biomedical Research, the prenatal screening test result will be stored for a period of 5 years after the analysis has been completed and, after such period has expired, it will be anonymised if you have not exercised your right to cancel this genetic data. Only the prenatal screening test results will be stored identified beyond the 5 years mentioned above, in those cases where it is necessary to safeguard your health, or that of your relatives.

You may exercise your rights of access, rectification, erasure, limitation of any specific processing, portability and opposition to the processing described by contacting the following address: NIMGenetics GENÓMICA Y MEDICINA S.L.: Parque Científico de Madrid, C/ Faraday, 7 Campus Cantoblanco, 28049 Madrid. In the event that you require additional information on the processing of your personal data, you may check the additional information on our website: https://www.nimgenetics.com/politica-de-privacidad/

Further use of the data

The results obtained may contribute to increase the analytical ability of the test and the current state of knowledge, with the resulting benefit for new studies. Therefore, NIMGenetics requests your consent to use your anonymous (without data on your name and surname) clinical information and results obtained for scientific publications, quality studies and databases in the health field, maintaining strict confidentiality about your identity, as it would be a completely anonymous use.

Likewise, NIMGenetics requests your consent for the transfer of your anonymised data (without any possibility of identifying you) to third parties for use in the field of scientific research.

NIMGenetics contact details

Feel free to contact NIMGenetics by telephone at +34 652893953 to clarify any doubts that may arise in connection with the content of this informed consent.

In order to carry out the requested prenatal screening test, you must sign and date the informed consent form.