NEXT BIOSCIENCES

Preimplantation Genetic Testing (PGT) Test Requisition Form

NG-CLI-PGT-FRM-001-REV-005 | 2024.05.01

Test information

- ☐ **PGT-A** (Preimplantation Genetic Testing for Aneuploidy) for comprehensive chromosome aneuploidy screening of chromosomes 1-22, X&Y.
- ☐ **PGT-SR** (Preimplantation Genetic Testing for Structural Rearrangements) for chromosome imbalance risk (translocation screening).
  - Karyotype to be sent for review by laboratory prior to testing.
- ☐ **PGT-M** (Preimplantation Genetic Testing for Monogenic Disorders) for single gene condition(s).
  - Requires a trophectoderm biopsy in conjunction with a frozen cycle (delayed embryo transfer).
  - PGT-M test optimisation to be discussed with laboratory prior to IVF treatment.

Reason for testing:

- ☐ Improve IVF
- ☐ Chromosomal rearrangement (karyotype to be sent for review prior to testing)
- ☐ Recurrent pregnancy loss
- ☐ Sex-linked genetic disorder
- ☐ AMA (advanced maternal age)
- ☐ History of chromosome anomalies (specify)
- ☐ Single gene disorder (specify)

Clinic information

Healthcare provider:	Contact no.:
Centre/clinic name:	Healthcare provider signature:
Patient file no.:	
IVF coordinator:	
Email for report:	Date: DD / MM / YYYY

Patient information

Patient		Partner	
Last name:		Last name:	
First name:		First name:	
Date of birth:	D D M M Y Y Y Y	Date of birth:	D D M M Y Y Y Y
ID/passport no:.		ID/passport no.:	
Patient sex:	Male ☐ Female ☐ Other ☐	Partner sex:	Male ☐ Female ☐ Other ☐
Email address:		Email address:	
Phone:		Phone:	
Address:			Postal code:

By signing this I declare that I have read, understood, and agreed to the contents of the informed consent agreement (on the back of this form) in its entirety and authorise Next Biosciences to analyse the DNA from my embryos and report the data to my healthcare providers.
I acknowledge and agree to the costs of the genetic testing, and agree to settle any and all invoices issued to me by Next Biosciences, by the stipulated date. I acknowledge that Next Biosciences will not release any results until payment has been made in full.

Patient signature:

Date: DD / MM / YYYY

Please send your form to **genetics@nextbio.co.za.**
For any queries, complaints or feedback, please contact us on **+27 (0)11 697 2900** or email us on **genetics@nextbio.co.za.**

GENERAL CONSENT – PREIMPLANTATION GENETIC TESTING

This consent provides information regarding the preimplantation genetic test(s) you are considering for embryos created via in vitro fertilisation (IVF), including: Preimplantation Genetic Testing for Aneuploidy (PGT-A), Preimplantation Genetic Testing for Monogenic Disorders (PGT-M), and/or Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR).

The potential risks, benefits, and limitations of preimplantation genetic testing should be discussed with your fertility healthcare provider.

Genetic counselling by a trained and certified counsellor is strongly recommended for all patients considering or proceeding with any genetic testing. An appointment with a genetic counsellor is available to you through Next Biosciences.

Preimplantation genetic testing is optional and you are not obligated to authorise such testing, even if recommended by your healthcare provider(s).

Genetic testing performed prior to implantation is not a substitute for routine prenatal testing ordered by your healthcare provider post implantation.

Signing this form and the relevant appendices indicates that you understand the risks, benefits, and limitations of the testing ordered, and provide informed consent for testing to be performed.

BACKGROUND

Chromosomes are structures located inside our cells that contain the genetic information (our genes) that make each human unique. Typically, an individual has 23 pairs of chromosomes for a total of 46 chromosomes (euploidy). One chromosome in each pair is inherited from the egg and the other is inherited from the sperm. Chromosome abnormalities can occur spontaneously during the maturation of the egg, maturation of the sperm, or during the process of embryo division after fertilisation. Any alteration to the number or structure of chromosomes, or to single genes within those chromosomes, may cause chromosome abnormalities that result in implantation failure, miscarriage, or the birth of a child with a genetic or genetically-influenced condition. Genetic testing of embryos prior to implantation for the presence of chromosome abnormalities may increase the chances of having a successful IVF outcome.

PREIMPLANTATION GENETIC TESTING PROCEDURE AND ASSOCIATED BENEFITS AND LIMITATIONS

Preimplantation genetic testing on an embryo sample is a multi-step procedure, which involves both your IVF clinic and the Next Biosciences testing laboratory.

EMBRYO BIOPSY AND ASSOCIATED RISKS:

- Following production of embryos by IVF, a sample of cells will be removed (biopsied) from the embryo(s) by your IVF clinic. Your IVF clinic will perform the biopsy at day five/six (a trophectoderm biopsy).
- While testing is performed, your embryos will be stored by your IVF clinic consistent with their internal policies and procedures.
- Because Next Biosciences is not involved in the biopsy procedure or initial sample identification, processing, and packing, Next Biosciences cannot guarantee that such steps will be performed optimally. As such, Next Biosciences is not responsible for any errors that may have occurred during such steps. This remains the responsibility of the IVF clinic. The IVF clinic's failure to perform biopsy and specimen preparation consistent with Next Biosciences' instructions and requirements may prevent the preimplantation genetic test(s) from being successfully performed. In this event, you indemnify Next Biosciences and hold it harmless from all loss, damage, or expense suffered by you, arising directly or indirectly out of any failure by the IVF clinic to properly perform a biopsy and/or specimen preparation for purposes of the genetic tests to be performed for you.

SAMPLE TRANSPORT AND ASSOCIATED RISKS:

- Biopsy samples will be sent by your IVF clinic to Next Biosciences via courier/driver.
- Next Biosciences is not responsible for delays or failures in transit due to factors outside of their reasonable control, including but not limited to weather or air travel conditions.
- Loss or damage of samples can occur and result in the inability to perform the test(s) or report test results.
- Specimen transport issues may impact our ability to perform the requested test(s). Next Biosciences retains the right to reject samples that do not meet its standards for testing.
- Insofar as our inability to perform the test(s) affects the timing of embryo transfer; Next Biosciences will not be liable to you for any risks or costs which might arise from a delay in the embryo transfer.

SAMPLE ANALYSIS AND RETENTION:

- Once we have obtained your biopsy sample for testing, the DNA is isolated from the cells and amplified to perform the test(s). It is possible that technical issues during these steps may prevent the test(s) from being performed.
- Only those tests which have been ordered by your healthcare provider and for which you have provided your informed consent and made payment for, will be performed on your sample.
- The initial biopsied cells are destroyed during the testing process and, therefore, cannot be returned to the embryo.
- Samples will typically be processed within ten working days of receipt. If indicated by the ordering provider, samples may be held for testing at a later time, in which event a storage fee will be charged.
- DNA derived from sample processing will be frozen and will be available for retesting and/or follow-up testing (upon request by your healthcare provider). After a ten-year period, our laboratory will discard any remaining DNA.
- In addition, you acknowledge and confirm that should you decide to have preimplantation testing performed by a laboratory other than Next Biosciences, after we have received and/or processed your sample, Next Biosciences will not transfer processed and/or stored samples for use at another laboratory due to protocol and liability concerns.

GENERAL RISKS AND LIMITATION OF LIABILITY:

- It is possible that intercourse may result in fertilisation and implantation, in addition to - or instead of - fertilisation and implantation from IVF. This would invalidate the results of any preimplantation testing.
- Additionally, all genetic testing has an inherent risk of discovering incidental findings in any individual included in testing. When discovered, incidental findings that are deemed to be potentially clinically significant will be reported to the ordering healthcare provider for additional evaluation as he/she deems appropriate.
- **You agree and accept that the maximum aggregate of all and any amounts which Next Biosciences may be liable for in respect of any claims arising from the testing services performed for you in terms of this Test Requisition Form (whether to you or any third party), will be limited to the amount paid by you to Next Biosciences for such testing services.**
- **You further indemnify Next Biosciences and hold it harmless from all loss, damage, or expenses which may be occasioned to you, arising directly or indirectly out of any genetic testing services which Next Biosciences performed for you under this Test Requisition Form.**

FINANCIAL CONSIDERATIONS, CANCELLATIONS, AND REFUNDS

Fees for genetic testing are in addition to any other costs associated with your IVF cycle and fertility treatment. Next Biosciences is entitled to full or partial payment in the event a test is started but is cancelled or not performed. You are liable for all costs incurred for genetic testing and should be fully aware of costing prior to testing, if you are unsure of costs the onus relies upon you to enquire.

CONFIDENTIALITY AND RESULTS DISCLOSURE:

- All information held about you in any form is strictly confidential. Next Biosciences will only send test results to the referring clinic and/-or healthcare provider, to such other parties you authorise us to send the results to, and as otherwise required by law. In the case of PGT-M, you consent to allowing Next Biosciences to share your confidential personal and other information required by the PGT-M laboratory to provide the services requested. PGT-M testing is done in collaboration with an international laboratory, either Cooper Genomics in the UK or USA or Bioarray in Spain. You acknowledge that you have read, understood, and agreed to the terms as specified in the appropriate laboratory's consent document, which may be accessed on their websites.
- You understand that the information collected is required by Next Biosciences and the PGT-M laboratory and that both parties are committed to protecting your personal information. The information is supplied voluntarily by you.
- Upon completion of your genetic testing, Next Biosciences may store test data to perform analysis for research purposes. Next Biosciences will remove all personal information from your test data prior to conducting such research studies and will not include your name or other personal information in the results of any research studies or publications. You consent to the use of your test data for this purpose and agree that you will not receive notice of such use and you will not receive any compensation nor derive any benefit from any commercial products or services which may be developed arising from such use.

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A)

TEST PURPOSE

The purpose of Preimplantation Genetic Testing for Aneuploidy (PGT-A) is to evaluate whether embryos have detectable chromosomal abnormalities or an abnormal number of chromosomes (aneuploidy). PGT-A does not screen for other conditions or diseases.

TECHNOLOGY:

- The test is performed using the Vitrolife EmbryoMap solution. This assay makes use of low coverage next generation sequencing (NGS) technology to screen embryo biopsy samples for large chromosomal copy number variations (CNVs) greater than 10 mega base pairs across the whole genome.
- The technology we use **CAN DETECT:**
  - Whole chromosomal gains or losses (aneuploidies such as trisomy, tetrasomy, monosomy, nullisomy)
  - Partial chromosomal gains or losses (duplications, deletions, insertions,unbalanced translocations)
  - Certain forms of polyploidy (entire additional set(s) of chromosomes)
- The technology we use **CANNOT DETECT**:
  - All forms of polyploidy
  - Balanced chromosomal rearrangements (translocations or inversions)
  - Small CNVs (microdeletions, microduplications) or single nucleotide mutations nucleotide mutations

MOSAICISM - REPORTING OF RESULTS:

- If testing is performed via NGS, we have the ability to report a sample's mosaicism. The term 'mosaicism' describes the occurrence of two or more genetically distinct populations of cells within an embryo biopsy sample. 'High level' denotes an estimated level of mosaicism >50%, and 'Low level' denotes and estimated level of mosaicism of 20-50%. Levels of mosaicism estimated to be lower than 20% are not reported. We report levels of mosaicism consistent with recommendations for interpreting mosaic results in accordance with international guidelines.
- The selection of embryos for transfer is at the discretion of your healthcare provider. The results provided to your ordering healthcare provider are intended as a guide. Additional information regarding mosaicism can be discussed with a genetic counsellor.

BENEFITS AND LIMITATIONS:

- Chromosomal abnormalities are one of the most common reasons for implantation failures and miscarriages that occur within the first 12 weeks of pregnancy. Reducing the likelihood of implanting a chromosomally abnormal embryo may reduce the risk of implantation failure and miscarriage.
- PGT-A is not 100% accurate. Should you wish to confirm the chromosome status of a resulting pregnancy, prenatal diagnostic testing will be required.
- Because the biopsy sample is only a very small sample of the entire embryo, it is possible that the chromosome complement identified via PGT-A will differ from the overall chromosome complement in other section(s) of the embryo (ie. more than one chromosomally distinct cell line is present within the same embryo).
- The clinical interpretation provided in the test results will be applicable to the date the sample is taken. The clinical interpretation of test results can change over time with emerging data and/or changes in professional organisation guidelines. Next Biosciences is under no obligation to update test results in response to these changes.
- Test results and interpretations are based solely on the identified chromosome composition and do not account for embryo quality or other factors affecting implantation and pregnancy. Please consult with your healthcare provider for additional information regarding factors that may impact, and/or diagnostic tests that may help you assess, the chances of implantation or successful pregnancy.
- **Favorable PGT-A results do not guarantee that a child will be born without any birth defect(s) or genetic disorder(s).**
- **PGT-A has an inherent risk of error or misdiagnosis. Thus, it is strongly recommended that if you become pregnant with an embryo tested by Next Biosciences, post-implantation diagnostic prenatal testing be performed by you to test the genetic status of the fetus.**
- Research into the clinical implications of mosaicism is ongoing, and while some studies have suggested that mosaicism may impact rates of implantation, ongoing pregnancy, and miscarriage, only you and your healthcare provider can decide whether and how to use information derived from test results for clinical decision- making. These results should be considered in conjunction with other factors that may impact upon your decision. In the event of mosaic results, a rebiopsy is not necessary or recommended.
- This form does not provide all of the information that may be necessary and/or important for you to understand your test results. Therefore, you should consult with your healthcare provider to determine whether or how you will use your test results in your family planning decisions.

PREIMPLANTATION GENETIC TESTING FOR MONOGENIC DISORDERS AND STRUCTURAL REARRANGEMENTS (PGT-M AND PGT-SR)

TEST PURPOSE

The purpose of Preimplantation Genetic Testing for Monogenic Disorders and Structural Rearrangements (PGT-M/PGT-SR) is to identify embryos prior to implantation that may contain single gene disorders or chromosome rearrangements already known to exist within one or both biological parents. Ordering healthcare providers may use information from this test to decide whether to use a particular embryo in future IVF treatment.

TECHNOLOGY

- Once the DNA has been amplified single gene mutation testing may be performed by linkage-based analysis, or linkage analysis combined with direct mutation testing. If the cell is found to be free of the mutation(s), then it is inferred that the embryo it was derived from is also free of the mutation(s).
- A genetic mutation report and/or karyotype verifying the mutation or rearrangement is required before testing can be performed. Testing will only be performed for mutations or rearrangements in the prospective parent(s) as indicated by the ordering healthcare provider and verified by the aforementioned reports.
- Depending upon the abnormality identified, testing for chromosome rearrangements can be performed via next generation sequencing (NGS) to determine if a balanced amount of genetic material (DNA) is present. A subset of gene disorders or chromosome rearrangements may not be detectable via NGS.

BENEFITS AND LIMITATIONS:

- Using the results of PGT-M/PGT-SR, your healthcare provider may be able to improve the chances that an implanted embryo will not have a specific genetic disease or chromosome rearrangement. The probability of becoming pregnant with an affected fetus is significantly smaller following preimplantation testing than it is after natural conception.
- Ideally, several embryos are generated during IVF to maximize the probability that at least one embryo without a detected mutation or chromosome rearrangement will be found during testing. It is possible that no embryos will be detected without a mutation or chromosome rearrangement.
- We will only perform PGT-M/PGT-SR concerning the specific mutation(s) or chromosome rearrangements that were ordered by your healthcare provider. Additional genetic disease mutations that might exist in an embryo that will not be tested as part of the PGT-M/PGT-SR service unless subsequently requested by the healthcare provider.
- The clinical interpretation provided in the test results will be applicable to the date the sample is taken.
- The clinical interpretation of test results can change over time with emerging data and/or changes in professional organisation guidelines. Next Biosciences is under no obligation to update test results in response to these changes.
- **PGT-M/PGT-SR has an inherent risk of error or misdiagnosis. Thus, it is strongly recommended that if you become pregnant with an embryo tested by Next Biosciences, post-implantation diagnostic prenatal testing be performed by you to test the genetic status of the fetus.**

COMPLIANCE WITH THE PROTECTION OF PERSONAL INFORMATION ACT (POPIA):

- You understand that Next Biosciences takes the privacy of its patients very seriously and has implemented reasonable security measures to guard against the unauthorised disclosure of your private patient information (personal information) in line with the Protection of Personal Information Act (POPIA), and as more fully provided for in the Privacy Policy available at: https://nextbio.co.za/Legal/Privacy-Policy.
- You acknowledge that your personal information may be disclosed to Next Biosciences personnel, or to Next Biosciences' its affiliates, sub-contractors and vendors, solely for the purposes of providing the testing services.
- You acknowledge that your personal information may be disclosed by Next Biosciences in response to a specific request by a law enforcement agency, subpoena, court order, or as required by law.
- You confirm that the personal information supplied by you is true and correct and that you are responsible for updating your information to ensure that it remains correct.
- You acknowledge that your personal information will be retained by Next Biosciences for the required retention periods applicable to the medical and healthcare industry.
- In providing the testing services to you, your personal information may be transferred outside of South Africa, which you agree and consent to. Next Biosciences has ensured that all information transferred is done in an encrypted format.
- Next Biosciences may from time to time provide you with marketing information relating to testing services which may be relevant to you personally. You agree and consent to Next Biosciences using your personal information for these purposes and to inform you about any changes to the testing services offered by any of the companies forming part of the Next Biosciences group of companies.
- By sharing personal information with Next Biosciences, you agree and consent to the use of your personal information as setout above and more fully set out in the Privacy Policy available at: https://nextbio.co.za/Legal/Privacy-Policy.
- You warrant that you are entitled to provide Next Biosciences with the information and data that you provide and you indemnify Next Biosciences against any claims of a data breach by a third party.