

## I. PRIOR INFORMATION FOR PATIENTS

The prePGT study includes a battery of genetic tests and studies that are performed on individuals/couples, and usually close relatives of these, in order to determine the most appropriate strategy to determine whether future embryos are carriers/affected by the specific genetic/cytogenetic disorder identified within the couple or the couple's family. These studies require genetic information from the patients undergoing PGT to maximize accuracy when analysing pre-embryos/ embryos.<sup>1</sup>

In the case of monogenic diseases, which are caused by a known variant in a particular gene, the attending physician may prescribe the test for Monogenic Diseases (PGT-M) in the context of assisted reproductive treatment (IVF). Before PGT-M is performed on pre-embryos, a prePGT-M test must be performed to examine the inheritance of the mutation using direct mutation testing and/or linkage analysis.

PrePGT can also be performed in couples in which one or both members of the couple carry microdeletions, microduplications or other chromosomal rearrangements (e.g. reciprocal translocations). In these cases, it may be necessary to perform preliminary studies to determine the strategy, studying the segments involved to evaluate whether it would be possible to detect such abnormalities with the NGS platform used for chromosome analysis. In cases where it is not possible to accurately detect the abnormalities by NGS, samples from other family members may also be necessary.

## II. WHEN ARE PREPGT STUDIES INDICATED

Every time we need to perform PGT-M in the pre-embryos to avoid the inheritance of a monogenic disorder prePGT-M study shall be performed. Additionally, a prePGT study will be required for some microdeletions, microduplications or other chromosomal rearrangements. This step is needed to set up the exact protocol for the disease or to check whether genetic abnormalities could be detected in the pre-embryos before starting the IVF+PGT cycle.

## III. PROCEDURE

The prePGT study results from the combination of the following milestones:

- Review of genetic reports previously carried out, both of the patients and of the relatives identified as necessary.
- Preliminary laboratory assessment of the case.
- Collection of biological samples to be analysed from patients and relatives.
- Receipt of samples from patients and relatives identified as necessary for the study.
- Analysis of samples received.
- Confirmation of the feasibility to identify the genetic condition studied and communication of the results to the reference clinic.

The length of time needed to complete the additional studies, prior to beginning a PGT cycle, is typically 40 working days. The time begins from the date on which Juno Genetics España has received all the necessary samples and paperwork (consent form, test request form). The samples required from patients and any relatives would have been communicated by Juno Genetics to the IVF clinic and/or genetic counsellor prior to the acceptance of the case. A small percentage of cases may suffer a variable delay due to technical challenges developing a test, which are often impossible to predict. Should this occur, Juno Genetics will notify the clinic about the delay as soon as possible.

The sample (usually blood or saliva) to be used in this genetic analysis will be obtained using standard techniques, with no, or very low risk, to health. The DNA obtained from this sample will be sent, together with your personal identification data and clinical information relevant to the analysis, to the Juno Genetics Laboratory in the USA.

## IV. RESULTS

After performing prePGT study we are mostly sure that we are able or not to detect the genetic/cytogenetic anomalies in the pre-embryos. Hence, once the prePGT is finished successfully, the IVF+PGT cycle could be started.

The results of the feasibility study for the PGT case will be communicated to the referring doctor/clinic.

## V. LIMITATIONS OF THE prePGT STUDIES. INCIDENTAL FINDINGS

Even when prePGT is carried out appropriately, and although the benefits of the test are usually considerable, there are limitations as described below.

The genetic tests to be performed shall be strictly limited to those necessary to detect the genetic/cytogenetic mutation/alteration/condition identified within the feasibility study. The information obtained during additional studies, carried out to support the development of a preimplantation genetic test, has no clinical or diagnostic value for the people who provided the

<sup>1</sup> In countries such as Spain, the legislation refers to in vitro embryos with less than 14 days of development as "pre-embryos", while in other countries the legislation defines them as "embryos" from the moment of fertilization, without making this distinction. For the purposes of genetic tests, there is no difference, since the biopsy to obtain the sample takes place between days 5 and 7 after fertilization.

samples, but it is necessary to perform the PGT test.

In PGT cases the accuracy may be affected if the information provided is erroneous in relation to the identification of the disease-causing variants, or in the biological relationship and genetic status of family members.

There is a risk that there may be other genetic conditions in patients or relatives that are not identified or that non-existing “de novo” mutations may arise in the embryo.

Other genetic/cytogenetic conditions may be detected during the study, although it is not the purpose of the study. This type of result is considered an incidental finding. Therefore, if the results suggest a genetic condition, then JUNO will contact your doctor to investigate this incidental finding and provide genetic counselling.

There is a small chance that the prePGT study will be inconclusive and therefore the subsequent PGT test cannot be offered

## VI. ECONOMIC INFORMATION

The prices and conditions governing the performance of these tests, if applicable, will be detailed to you at the centre where you are being attended.

JUNO laboratory does not directly provide prePGT studies to patients, therefore, it cannot provide any quotes or approximate costs for this service under any circumstances.

## VII. GENERAL LEGAL ASPECTS RELATED TO ASSISTED REPRODUCTION AND SPECIFIC ASPECTS RELATED TO THE REQUESTED TEST

The biological sample submitted, along with the necessary personal data for the provision of the service, will be sent for analysis in a coordinated manner between the laboratories of Juno Genetics España, located at Ronda de Guglielmo Marconi, 11-A, 1º 22B, 46980 Paterna (Valencia), and Juno Genetics, US Inc., located at 140 Allen Road, Suite 300, Basking Ridge, NJ 07920 (USA). The genetic analysis of the sample will be carried out in accordance with the applicable Spanish regulations, primarily Law 14/2006 on Assisted Human Reproduction Techniques and Law 14/2007 on Biomedical Research.

However, please be informed that in the event of any temporary impediment or incident occurring in this Laboratory that could delay the result of your test (e.g., equipment breakdown in genetic analysis, technical maintenance shutdowns, interruptions in the supply of resources, etc.), in order to provide the committed service and obtain the analysis result in the shortest possible time, your sample and necessary personal data for the provision of the service will be sent to Juno Genetics Ltd., Hayakawa Building, Edmund Halley Road, Oxford Science Park, Oxford OX4 4GB, United Kingdom, at no additional cost. If this is the case, it will be noted in the report that will be provided to you regarding the analysis result of your sample issued by this Laboratory, which will have conducted the test in accordance with the provisions of the Human Tissue Act of 2004.

In the event that some or all of the tests cannot be carried out in any of the above laboratories, Juno Genetics reserves the right to carry out the analyses through a reference laboratory. This circumstance will be indicated in the final report issued.

In any case, the 1997 Oviedo Convention on Human Rights and Biomedicine will apply, relevant in that it limits medical and research diagnosis of genetic conditions only when the subject receives appropriate genetic counselling.

If the performance of this test has been indicated from a country other than Spain, the professional or clinic requesting the test will be responsible for ensuring that both the test itself and its application in the specific case is in accordance with the stipulations of its national or regional regulations, as well as for informing the subject of the test of any particularly relevant issue that such legislation contemplates.

## VIII. DATA PRIVACY, STORAGE AND USE FOR THE STUDY OF SAMPLES

Patient and donor privacy is a top priority at Juno Genetics. All personal information and genetic results are strictly confidential. The only individuals who can access this information are the personnel at the reproductive clinic, the Juno Genetics Laboratory analysing the sample, and the relevant authorities if required by the laws of the applicable jurisdiction.

In accordance with the current data protection regulations, such as the EU General Data Protection Regulation (EU2016/679) and national data protection laws including the Spanish Organic Law 3/2018 on the Protection of Personal Data and Guarantee of Digital Rights, and, where applicable, the UK Data Protection Act 2018, you have the right to exercise your rights, if desired, including the right to access, rectify, erase, and revoke your consent, as well as the right to restrict processing, data portability, and to not be subject to automated decision-making based solely on your data. These rights can be exercised by contacting the following postal address:

- Juno Genetics España, S. L., Parque tecnológico de Paterna (46980), Valencia, Spain, Ronda de Guglielmo Marconi, 11, edificio A, segunda planta, locales A-1-2 y A-2-2 (in case your analysis is carried out in this Laboratory).
- Juno Genetics Ltd., Hayakawa Building, Edmund Halley Road, Oxford Science Park, Oxford OX4 4GB, United Kingdom (in exceptional circumstances as stated in this document, if your analysis is carried out at this laboratory).
- In both cases, you can also contact the Juno Genetics DPO (Data Protection Officer) at: [Juno.DPO@junogenetics.com](mailto:Juno.DPO@junogenetics.com)

As part of the prePGT genetic test, it is necessary to send personal data and biological samples to the group's laboratory in the United States. We would like to assure you that this processing will be carried out in accordance with the highest standards of confidentiality and security, guaranteed by the application of standard contractual clauses approved by the European Commission

to ensure a level of protection equivalent to that required by the GDPR. If you consider that your rights have been violated, you may lodge a complaint with the Spanish Data Protection Agency ([www.aepd.es](http://www.aepd.es)).

Personal data will only be processed for the following purposes: (1) fulfilling obligations arising from the requested services (legitimate basis under Art. 6(1)(b) and 9(2)(h) of the GDPR); (2) reviewing and ensuring the quality of the provided services (internal audits, quality controls, laboratory validation studies based on Art. 6(1)(f) of the GDPR); (3) educational/training purposes, always subject to anonymization prior to use to prevent identification of the patient in question; (4) research purposes, scientific publications, and presentations, always subject to prior anonymization to ensure non-identifiability of individuals. Research will be conducted in compliance with the General Data Protection Regulation and national data protection laws. (5) providing personalized responses to inquiries or suggestions from patients requesting the test and ensuring that the test has been carried out correctly and addressing any concerns (legitimate basis under Art. 6(1)(b) of the GDPR); and (6) monitoring patients in the future to obtain feedback on the service received (legitimate basis under Art. 6(1)(f) of the GDPR). Data will be stored for a minimum of five years unless local laws in the applicable jurisdiction state otherwise. Finally, if you believe that your data protection rights have been violated, you have the right to lodge a complaint with the competent Data Protection Authority.

In addition to the above, Juno Genetics will distribute your test results only to your physician, unless specified in writing by you (or a person legally authorized to act on your behalf) or required by a court of law.

## Recipients of the data

In order to improve research and development in assisted reproduction techniques, other centres or entities within the group may have access to personal and genetic data in cases where information derived from the tests performed may be used in clinical studies by any of these entities, in accordance with the General Data Protection Regulation and national data protection laws. It is important to note that any data that may reveal your personal identity and/or that of your family will be anonymised, treated with absolute confidentiality, and used only for research and development purposes related to the services provided by the group. Necessary security measures will be implemented to ensure the security and confidentiality of your data.

Regarding the communication of data for research and development purposes:

- ☐ YES, I want Juno Genetics to share my information for research and development purposes.
- ☐ NO, I do not want Juno Genetics to share my information for research and development purposes.

## IX. AUTHORIZATION TO USE SURPLUS OR DISCARDED SAMPLES FOR THE OPTIMIZATION AND VALIDATION OF NEW TESTS

It is important for Juno Genetics to be able to use surplus or discarded samples for the optimization and validation of new tests and the development of new analysis methodologies, including new technologies based on the development of Artificial Intelligence applications, so that these advancements and improvements can benefit future couples, including your case. The surplus samples used for this purpose would be anonymized and processed blindly, ensuring that no findings can be reported to you. This would only take place in Juno Genetics' laboratory.

Clinical results, information, and raw data may be reviewed and/or reanalysed for future publications and scientific presentations. At all times, these data will be subject to prior anonymization, ensuring that personal identification is not possible under any circumstances. All treatments and processes will be carried out in accordance with the General Data Protection Regulation and national data protection laws.

I also understand that Juno Genetics may use the resulting information for scientific publications of results and their presentation after anonymizing any personal information.

I understand and accept that, since all information will have been previously anonymized, I will not be able to access new results or findings in the present or future, nor will I receive any financial benefits from publications and presentations, nor will I be compensated for products developed as a result of these activities.

## X. ONCE READ AND UNDERSTOOD THE ABOVE, I AM INFORMED OF:

- I have been informed that I am not obliged to undergo this genetic analysis and I therefore freely and voluntarily consent to it being carried out.
- The indication, procedure, likelihood of success, limitations, risks and complications of the proposed test.
- My test results may have implications for other members of my family. I acknowledge that my results may sometimes be used to provide appropriate medical care for others. This may be done by discussing it with me, or in such a way that I am not personally identified in this process.
- I understand that these procedures may be cancelled at any time during their performance, either for medical reasons or at the request of the person concerned, provided that no harm is done to the patients.
- Normal practice in genetic testing laboratories is to store DNA extracted from samples received even after the current test is completed. My sample could be used as a "quality control" for other tests, e.g. that of family members. The methodology of extracting the DNA or the "raw data" generated may make it unfeasible for use by third party laboratories.
- Both my test results and my test report will become part of my patient file.

- I hereby inform of the availability of the health staff of this centre to expand on any aspect of the information that has not been sufficiently clarified.

I understood the explanations given to me in clear and simple language. In the case that the test was performed in the context of assisted reproduction treatment, the doctor who attended me at the clinic where I am patient allowed me to make all the observations, clarified all the doubts I had and explained the implications of the possible results of the test.

I also understand that at any time and without the need to provide any explanation, I can revoke the consent I am now giving. However, please note that, depending on when the test is revoked, you may have to pay for any costs associated with the test that have already been incurred prior to the revocation. Mainly the materials and reagents associated with the test, as well as the costs of transporting the samples.

I therefore declare that I am satisfied with the information I have received and that I understand the scope and risks of the processing.

# XI. PATIENT AND AUTHORISED HEALTHCARE PROFESSIONAL INFORMATION

Patient name	ID number PATIENT (if apply)	Patient Date of Birth (DOB)

Address of PATIENT

If the patient is a minor, this consent must be signed by the minor's legal representative or guardian

Name of Legal Guardian	ID number Legal guardian	Legal guardian Date of birth (DOB)

Address of Legal Guardian

## Authorisation:

After reading the COMPLETE document, I authorise the staff of the Reproduction Unit to carry out the feasibility study prior to the proposed preimplantation genetic testing for monogenic diseases and/or structural rearrangements.

## Signature and date

Name of the AUTHORIZED HEALTHCARE PERSONNEL	Professional Registration Number	Date and signature

## I declare that:

I have explained the content of these tests and their risks, and clarified any doubts and questions raised by the individual. Furthermore, I commit to providing the necessary genetic counselling based on the test results.