I. GENERAL INFORMATION FOR PATIENTS OR DONORS

Information about hereditary disorders and the Geneseeker test

Disorders that can affect the fetus during pregnancy or be diagnosed after birth can be broadly classified as acquired (due to external factors) or genetic. Genetic disorders occur due to changes or alterations in our genes. Genes are small instructions found in our cells that determine how our body develops and functions. These instructions are written in a molecule called DNA. There are different types of genetic diseases. Some genetic diseases can occur due to spontaneous changes in genes, without being inherited. These spontaneous genetic changes are known as de novo mutations. Other genetic diseases are hereditary, which means they are passed down from parents to children through genes. Currently, over 7,000 hereditary disorders have been described. Hereditary genetic diseases can be autosomal when caused by changes in genes found on non-sex chromosomes (chromosomes common to males and females), or they can be X-linked when the altered genes are located on the X chromosome, one of the two sex chromosomes (males have one X chromosome and one Y chromosome, while females have two X chromosomes). In turn, genetic diseases can be classified as dominant or recessive. In dominant disorders, the presence of a single altered copy of the gene is sufficient to develop the disease. In recessive diseases, two altered copies of a specific gene are required to develop the disease. Conversely, individuals with a single altered copy of the gene are considered carriers of the disease. Carriers of autosomal recessive diseases are not typically expected to develop symptoms associated with the disease. However, if their partner is also a carrier of the same disorder, their offspring would have a 25% risk of inheriting 2 altered copies of the gene and, therefore, the disease.

It is important to note that mutations affecting genes on the X chromosome are usually recessive in females (as females have two copies of the X chromosome). If a woman is a carrier of a mutation on the X chromosome, on average, 50% of her male children will be affected by a hereditary disorder. However, males only have one copy of the X chromosome, and therefore, if they inherit a defective gene on this chromosome, they will not have any functioning copy of the gene, which could lead to the development of symptoms of a hereditary disorder.

The GeneSeeker test is a carrier genetic study that allows for the analysis of thousands of mutations responsible for hundreds of severe autosomal recessive and X-linked hereditary disorders. Through the GeneSeeker test, a person's carrier status for specific genetic diseases can be identified. It is not uncommon to discover that we are carriers of a mutated gene, even when there is no family history of genetic disease. In fact, recent scientific studies estimate that, on average, most individuals are healthy carriers of two or three diseases.

When the GeneSeeker test is performed preconceptionally on men and women who wish to have children using their own reproductive cells, the results can help identify couples with a particularly high risk of transmitting a genetic disorder to their offspring. In the face of such results, there are several options available to reduce the risk of having an affected child, including preimplantation genetic testing (PGT), prenatal testing, or other solutions designed to mitigate the risk.

In couples who are considering reproductive treatment using donated gametes (eggs or sperm), performing the GeneSeeker test on the patient who will use their own gametes allows for the selection of donors without matches in the diseases they carry. This way, the reproductive risk for the couples is reduced.

In the case of gamete donations, the GeneSeeker test allows for the study of donors to identify if there are genetic mutations with the potential to cause hereditary disorders in offspring conceived with those donated gametes. Except in exceptional cases, the information obtained through the GeneSeeker test is not medically relevant for the donors. This is because the majority of the detected mutations are associated with recessive diseases, and therefore, these mutations are not associated with any symptoms. However, the information obtained could be relevant in the future when planning to have one's own children. One way for IVF clinics and donor banks to increase the chances of a healthy pregnancy and to detect the risk of transmitting certain mutations associated with serious disorders is to offer the GeneSeeker test to their patients and perform it on the donors.

II. LIST OF GENES - VARIANTS ANALYSED BY GENESEEKER

The GeneSeeker test does not study all the genes in the human genome, nor does it examine all possible variants within the genes it analyses. This will vary depending on the chosen gene panel. You can find a breakdown of the genes and variants analysed in the GeneSeeker and GeneSeeker Essential tests on the website provided below:

https://junogenetics.eu/our-tests/gene-seeker/

The list of genes, their variants, and their impact on health may be subject to changes in the future based on an improved understanding by the scientific community. The results presented in the reports reflect the best possible outcome based on the most up-to-date information available at the time of the test.

III. FOR WHO AND IN WHICH CASES IS THE GENESEEKER TEST INDICATED?

The test can be used by couples to determine their risk of transmitting certain mutations associated with severe disorders.

This test is particularly recommended by IVF clinics, gamete banks, and laboratories for couples at high risk of inheriting recessive Mendelian disorders, such as individuals from communities with high levels of consanguinity.

It can also be used to determine if gamete donors are carriers, in order to ensure compatibility with the recipient and minimize the risk of conceiving children affected by these disorders.

This test can also be performed on healthy couples who are not affected by any genetic disorder but have a family history of genetically inherited diseases. They may choose to undergo the test to minimize the risk of transmitting certain mutations associated with serious conditions to their children.

Similarly, in healthy couples with no family history of genetic disorders or with unknown family history, the test can also help minimize the risk of transmitting these mutations to their offspring.

IV. PROCEDURE

For the GeneSeeker analysis, a blood sample will be obtained using standard techniques, which pose minimal or no risk to health. Only in specifically agreed cases, the sample collection may be done using saliva or buccal swabs.

Once the genetic test is performed, the samples will be preserved so that further analysis can be conducted and results can be verified if necessary.

The test is performed as follows:

1. We collect a blood sample.
2. The DNA is extracted from the cells of the received sample.
3. The DNA is analysed using a technology called "next-generation sequencing" (NGS), which examines the genetic regions where mutations are commonly found. You can find an updated list of the genes examined on the JUNO GENETICS website (refer to Section II of this document for more information).
4. Additional testing is also conducted on certain genes, depending on the selected test (e.g., *CYP21A2, HBA1/2, SMN1, DMD, F8*, and *FMR1*). You can find an updated list on the JUNO GENETICS website (refer to Section II of this document for more information).
5. The data obtained through NGS is analysed by JUNO GENETICS' specialized personnel and computer systems. They are compared with reference values from our databases to help distinguish between normal variations in DNA sequence and mutations responsible for inherited disorders.
6. The results are provided in a report. If patients undergo assisted reproductive treatment using their own gametes (eggs + sperm), the medical team will use the test information to perform a genetic comparison and ensure that both individuals do not have the same affected genes. If they do have affected genes in common, the medical team will conduct a genetic consultation to explore alternative solutions, such as preimplantation genetic testing of embryos (PGT). If patients undergo assisted reproductive treatment with a gamete donor, the medical team will use the information to select the most suitable donor and avoid selecting a donor with the same affected genes.

V. RESULTS

The results of genetic tests and analyses should be interpreted in the context of additional laboratory tests, family history, and other clinical findings. We recommend genetic counselling to evaluate the implications of the test results.

The results of the GeneSeeker test may include the following:

+ MUTATION NOT DETECTED:
In the genes analysed, no mutations have been found that could cause an inherited disease. This significantly reduces the probability of a future child being affected by a disorder associated with the analysed genes. However, it is important to note that the test cannot detect all possible mutations in the analysed genes, and therefore, the risk is not zero. Please refer to the limitations of the test below for further information.

+ DETECTED MUTATION (for autosomal recessive disorders):
A variation in the DNA sequence (a mutation) has been identified in one or more of the genes analysed. In most cases, this result will not have direct clinical consequences for the carrier themselves. However, for each gene with a mutation, there is a 50% chance that the faulty copy of the gene will be passed on to a child. If the other parent also has a mutation in the same gene, there is a high risk of the couple's children being affected by a genetic disorder (approximately a 25% risk per gene when both parents are carriers of the mutation). We recommend this test to any couple who is planning to start a family or to any gamete donor to obtain more information about the risk of having a child with a genetic disorder.

It is strongly recommended that the results of this test be discussed with a genetic counsellor or another qualified healthcare professional so that the health implications of any detected mutation can be fully understood.

+ MUTATION DETECTED (for X-linked diseases in female patients):
A variation in the DNA sequence (a mutation) has been detected in one or more of the examined genes. In most cases, this result does not have direct clinical consequences for the carrier individual. However, for each gene with a mutation, there is a 50% probability that the defective gene copy will be transmitted to offspring. It is expected that male children inheriting the mutation will develop an inherited disorder, and in some cases, daughters may also exhibit symptoms. It is strongly recommended to consult the results of this test with a genetic counselor or other qualified healthcare professional to fully understand the health implications of the detected mutations.

+ No result (NO Call):

List of variants for which a result could not be obtained due to insufficient or poor-quality DNA sequencing.

VI. LIMITATIONS OF THE GENESEEKER TEST AND IMPORTANT APECTS TO BE TAKEN INTO CONSIDERATION

It should be noted that GeneSeeker may not be able to accurately analyse all mutations. Any mutation for which we were unable to obtain appropriate results will be included in the GeneSeeker report provided by JUNO GENETICS as "No Call." These mutations should be considered as not analysed.

The NGS technology we use for this test does not allow us to identify all possible mutations. For example, we cannot identify mutations resulting from significant DNA rearrangements (deletions, insertions, or large inversions), nor can we detect triplet nucleotide expansions or mutations in gene regions that are not being studied.

Although GeneSeeker analyses many genes responsible for hereditary conditions, it is important to note that there are other genes not analysed by GeneSeeker that can also cause hereditary disorders. Additionally, while GeneSeeker can identify many of the common mutations in the genes it analyses, it does not evaluate the entirety of each gene and cannot identify all possible mutations. Although rare, it is possible for GeneSeeker to miss a mutation, even when specifically searching for it. Therefore, it is still possible for a couple (or a patient and a sperm/egg donor) to have a child affected by a disorder, even if GeneSeeker indicates their risk of having children with hereditary disorders is low.

Mitochondrial diseases and disorders with a dominant, multifactorial, or digenic inheritance pattern are not analysed with GeneSeeker unless otherwise specified. It is unlikely to detect mutations that are present in some cells of the body but not in all (known as "mosaicism"). If the germ line cells (sperm or eggs) are affected by mosaicism, there is a risk of transmission to offspring.

While the vast majority of mutations identified by GeneSeeker are recessive, some mutations can behave in a "dominant" manner, meaning that a carrier of the mutation may exhibit clinical symptoms or be at risk of developing them in the future.

GeneSeeker identifies a series of mutations that affect genes on the X chromosome. These mutations are of primary interest when it comes to producing male offspring, as they only have one copy of the X chromosome and do not have a second copy of any genes that can compensate for the functions of the mutated gene. However, in some cases, carriers of a mutated gene on the X chromosome or their daughters may exhibit some symptoms of the disorder.

It is important to note that the interpretation of variants is based on medical evidence and the latest scientific advancements. Therefore, the interpretation of variants is a dynamic process that can change over time as more evidence becomes available. Additionally, certain variants are classified as "variants of uncertain significance" (VUS), where the association with disease risk is unclear at the time of analysis. GeneSeeker only reports pathogenic and likely pathogenic variants, not VUS.

The presence of low-frequency polymorphisms (rare variations in the DNA sequence) can sometimes hinder the analysis of one copy of a gene, which means that we can only obtain results from the other copy. Similarly, the presence of pseudogenes (DNA sequence regions that appear very similar to a gene) can also confuse the analysis. Both circumstances can lead to false negatives or false positives.

GeneSeeker is highly reliable (>99% accuracy for the analysed mutations), but there are numerous factors that can affect the accuracy of the results, some of which are described above. Like any laboratory test, there is a small possibility of inaccurate results due to human errors during sample collection or processing, faulty laboratory equipment or materials, contamination of samples with other cells or external genetic material, non-compliance with pre-analytical conditions established to ensure result validity, etc. Therefore, the results should not be considered definitive and should always be analysed in combination with other test results and/or additional medical information.

It is considered that couples without mutations in the same genes have a low risk of having children with disorders, but the risk is not zero. Similarly, using the data obtained through GeneSeeker to avoid combinations of patients and donors with mutations in the same gene will reduce the likelihood of having affected offspring, although it cannot completely eliminate it.

There are certain medical reasons why GeneSeeker may not be suitable for some patients, and doctors should consider them before recommending/requesting the test. One example is chimeras, which occur when cells from two genetically different individuals are found within the body of the person undergoing the test. This condition can be congenital (usually as a result of a rare fusion of two twin embryos at a very early stage of development), or it can develop temporarily (e.g., through a blood transfusion) or permanently (e.g., as a result of a bone marrow transplant). It is important to note that these circumstances are likely to produce unreliable results. Using a saliva sample

instead of blood may help obtain more accurate results in certain situations, but it is not recommended for all cases. JUNO GENETICS can provide more information upon request.

VII. ACCESS TO GENESEEKER TEST RESULTS

Recipients of the chosen test results

Regarding the results of my GeneSeeker test, my preference is as follows: (choose one of the following options)

☐ **YES, I do want to receive the final conclusions**: I wish for the clinic where I have requested the GeneSeeker test to inform me of their conclusions, understanding that these results may reveal information about my risk of developing one or more of the serious disorders analysed and/or my risk of transmitting genetic abnormalities to my children, even if I currently do not show any symptoms of such disorders. The results of the GeneSeeker test will be available and delivered within approximately 4 weeks. Around 2% of the samples may require an additional 7 calendar days to confirm certain mutations.

☐ **I do NOT want to receive any type of information**: I do not wish to have access to my results, nor do I want to receive any information about them. However, I understand that if the information is necessary to prevent serious harm to my health, myself or a legally authorized representative may be informed in accordance with Article 49.2 of Law 14/2007. In any case, communication will be limited exclusively to the information necessary for that purpose. Please provide the contact details of the authorized person or representative who should be contacted for the aforementioned purposes.

Notification of results following test expansion

If in the future the panel of genes and/or variants that were initially reported to you is expanded, this would be done by analyzing the raw data already obtained through the previous genetic analysis,

My preference would be as follows (choose one of the following options):

☐ **I would like** the medical team to contact me to inform me of the updated results. In the event that the list of genes and/or variants analysed is expanded, I would like to be informed about the new list of genes and variants analysed.

☐ **I would prefer not** to receive any new information regarding additional findings. However, I understand that if the information is necessary to prevent serious harm to my health or that of my family members, I may be informed or a legally authorized representative may be informed. In any case, communication will be limited solely to the information necessary for that purpose.

Please provide the contact details of the authorized person or representative to be contacted for the aforementioned purposes.

In any case, I declare that I have received appropriate genetic counselling from qualified personnel at the clinic I have visited. They provided me with information about the significance of the test, including the possible options that may be offered based on the results obtained, and I understand that they are available to address any questions I may have and provide additional genetic counselling that I may require once the results of my GeneSeeker test are available.

Taking into account my medical history and that of my close family, if I suspect that either I or any of my close relatives may have a hereditary disorder, or if I am aware of any diagnosis or test result that may indicate an increased risk, I commit to notifying the advising physician immediately. This is important as the GeneSeeker test may not specifically search for the potential mutation present in my family, which could result in a false negative.

VIII. ECONOMIC INFORMATION

The prices and conditions applicable to the performance of these tests, if any, will be explained at the centre you have indicated for GeneSeeker.

JUNO GENETICS laboratory does not directly offer the GeneSeeker test to patients, so they will not be able to provide any quotes or approximate costs for the service.

IX. GENERAL LEGAL ASPECTS OF ASSISTED REPRODUCTION AND SPECIFIC DETAILS ABOUT CARRIER SCREENING TESTS

The biological sample submitted, along with the necessary personal data for the provision of the service, will be sent for analysis to the facilities of Juno Genetics Spain, S.L., at Parque Tecnológico de Paterna (46980), Valencia, Spain, Ronda de Guglielmo Marconi, 11, Building A, second floor, premises A-1-2 and A-2-2. 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., 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 part or all of the tests cannot be performed in any of the aforementioned laboratories, JUNO GENETICS reserves the right to perform the analysis in another laboratory within the European Union, which offers the highest standards of quality and confidentiality in the handling of samples and the obtained results. This situation will be communicated to you in the final report issued.

In any case, the provisions of the Convention on Human Rights and Biomedicine (Oviedo Convention) of 1997 shall apply, as it restricts the genetic diagnosis and research of genetic conditions only when the subject receives appropriate genetic counselling.

In the event that the performance of this test has been requested from a country other than Spain, the professional or clinic making the request will be responsible for ensuring that both the test itself and its application in the specific case comply with the regulations of their national or regional legislation, as well as informing the test subject of any particularly relevant matters stipulated by such legislation.

X. DATA PRIVACY, STORAGE, AND USE FOR SAMPLE STUDY

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 analyzing 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 (if your analysis is carried out at 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

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 only distribute test results to your physician unless otherwise 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 anonymized, 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 in JUNO GENETICS companies:

☐ YES, I wish for JUNO GENETICS to share my information for research and development purposes.

☐ NO, I do not wish for JUNO GENETICS to share my information for research and development purposes.

XI. 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. We will only use these samples for this purpose if you authorize us to do so, and they will always be used anonymously and blindly, so it will not be possible to inform you of any findings. This will only be carried out in the 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.

XII. ONCE READ AND UNDERSTOOD THE ABOVE, WE ARE INFORMED OF:

- I have been informed that I have no obligation to undergo this genetic analysis, and I give my consent freely and voluntarily.
- I am aware of the suitability, procedure, purpose, limitations, risks, and complications of the proposed genetic screening test.
- The results of my test may reveal a variant of uncertain significance (VUS). My information may be shared to determine if such a variant is significant, including comparisons with the same variant in other patients, both in Spain and other countries. Any shared data will be anonymized so that it cannot be linked to any patient. I acknowledge that the interpretation of my results may evolve over time as more evidence is obtained from other cases.
- The results of this test may be analysed by the fertility clinic or the donor bank to compare the genetic profiles of patients or donors to confirm the absence of mutations in the same genes.
- Procedures may be cancelled at any stage, either for medical reasons or at the request of the test subject.
- It is common practice in genetic analysis laboratories to store the extracted DNA from samples, even after the completion of the current test. Once validated, my sample may be used as a "quality control" in other genetic tests. The DNA extraction methodology or the "raw data" generated by laboratory equipment may render its use by third-party laboratories unfeasible.
- Both the results of my tests and the corresponding report will be included in my patient record.
- The healthcare professionals who have attended to me are available to provide any additional information that may not have been fully clarified.

I have understood the information that has been explained to me in clear and simple language. If the test has been conducted in the context of assisted reproduction treatment, the doctor I have consulted with at the clinic where I am a patient has allowed me to ask all the necessary questions, clarified any doubts I had, and explained the implications of potential test results.

I also understand that I can withdraw the consent I am giving here at any time without the need to provide explanations. Therefore, I declare that I am satisfied with the information I have received and that I understand the scope and risks of the treatment.

SPECIFIC INFORMATION FOR DONORS:

- I have been informed that the genetic profile obtained from the blood analysis is primarily used to assess the compatibility of donated gametes with the intended recipients of the donation.
- In some cases, the identified genetic profiles may render the use of donated gametes unfeasible in any donation process. For example, mutations identified in genes located on the X chromosome. In such cases, the Fertility Clinic or Donor Bank may exclude you as a donor.
- Please note that the refusal to undergo this genetic analysis cannot automatically result in your exclusion from the donation program of the Fertility Clinic or Donor Bank you are participating in.

XIII. PATIENT AND AUTHORIZED HEALTHCARE PROFESSIONAL INFORMATION

PATIENT's Name	PATIENT's Identification Number	PATIENT's Date of Birth

Patient's Address

Authorization:

After reading the ENTIRE document, consisting of a total of 7 pages and 13 (XIII) sections, I authorize the staff of JUNO GENETICS ESPAÑA to perform the proposed carrier testing on my sample, for the chosen gene/variant panel.
Signature and Date

Name of the AUTHORIZED HEALTHCARE PROFESSIONAL	Registration Number	Date and Signature

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