Blank space reserved for IGENOMIX use only

igenomix
PIONEERS IN REPRODUCTIVE GENETICS

Test Requisition Form CGT 250/600

The fields marked with * are required to carry out the test

*Select a product

☐ **CGT/600**

☐ **CGT/250**

CGT/600: Analyses 547 genes using Next Generation Sequencing (NGS) and specific tests, linked to more than 600 diseases.

CGT/250: Analyses 250 genes using Next Generation Sequencing (NGS) and specific tests associated with the most prevalent disorders.

*Referring Doctor

*Clinic

01 Patient 1 information (fill out or attach label)

***Name** ***Surname(s)** ***Date of birth**

Unique Patient ID

*** Male** ☐ *** Female** ☐

Ethnic group (please indicate)

☐ Caucasian ☐ South Asian ☐ East Asian ☐ Arab ☐ Ashkenazi

☐ Hispanic ☐ Romani ☐ Afro-_____

If belonging to more than one ethnic group please indicate which _____

02 Patient 1 clinical information

***Date of sample collection** ☐ ***DONOR (tick if yes)**

Sample reference To be filled out at IGENOMIX

***Relevant clinical information for the test**

☐ Bone marrow transplant ☐ Blood transfusion (<60 days)

☐ Congenital or acquired chimera ☐ N/A

***Indication of test**

☐ No Family History ☐ With Family History[1]

☐ Known Carrier[1]

(i) Specify condition _____

Fill out 3 and 4 if two samples are submitted

03 Patient 2 information (fill out or attach label)

***Name** ***Surname(s)** ***Date of birth**

Unique Patient ID

*** Male** ☐ *** Female** ☐

Ethnic group (highly advisable to indicate)

☐ Caucasian ☐ South Asian ☐ East Asian ☐ Arab ☐ Ashkenazi

☐ Hispanic ☐ Romani ☐ Afro-_____

If belonging to more than one ethnic group please indicate which _____

04 Patient 2 clinical information

***Date of sample collection** ☐ ***DONOR (tick if yes)**

Sample reference To be filled out at IGENOMIX

*** Relevant clinical information for the test**

☐ Bone marrow transplant ☐ Blood transfusion (<60 days)

☐ Congenital or acquired chimera ☐ N/A

*** Indication of test**

☐ No Family History ☐ With Family History[1]

☐ Known Carrier[1]

(i) Specify condition _____

05 If your partner has previously taken a CGT test, please fill out the following fields

Name **Unique Patient ID/Sample Ref.**

06 Signature of patients 1+2

By signing this application form, I voluntarily ask Igenomix to perform the test indicated above. I have read and received a copy of the informed consent included in these pages. I have also been adequately informed of the risks, benefits and limitations of this test.

***Signature of Patient 1** ***Signature of Patient 2**

Date **Date**

***Email of Patient 1**

***Email of Patient 2**

07 Authorization from doctor / genetic counsellor

I certify that the patient and prescribing doctor's details given in this request form are accurate to the best of my knowledge and that I have requested the test indicated above based on my professional criteria. I have explained the limitations of this test and have answered any questions based on medical judgement. I understand that Igenomix may require further information and I agree to provide this information if necessary.

***Doctor's signature**

Date

***Doctor's email address for delivery of results**

INFORMED CONSENT FOR THE CARRIER GENETIC TEST CGT600/CGT250

DESCRIPTION, PURPOSE AND ADVANTAGES OF ANALYSES

The primary function of the Carrier Genetic Test or CGT is to limit the genetic risk in offspring, reducing the risk of transmission of autosomal recessive and X-linked disorders included in the test. Currently, around 5,000 diseases caused by the alteration of specific genes are known.

Each person has approximately 20,000 different genes. Scientific studies estimate that most healthy people, on average, are carriers of 1 or 2 mutations that can lead to severe genetic disorders in offspring. In most cases, carriers show no symptoms. In order for the symptoms of recessive disorders to develop, it is necessary for the two copies of a gene inherited by an individual (the one inherited from the father and the one inherited from the mother) to be altered.

To assess the risk of offspring being affected by these disorders, it is necessary to analyse which mutations are present in each person (and in which genes they are found) that can be transmitted to their offspring through their gametes (patients and donors). The aim of the test is to be able to compare and verify that the reproductive couple does not share mutations in the same autosomal recessive gene, in which case there is a high risk (25%) of offspring developing the disorder. Additional tests will be carried out on genes in women linked to the X chromosome that could lead to affected male offspring.

This test is recommended in assisted reproductive treatment but is also clinically valid in natural means of reproduction.

PROCEDURES, RISKS AND LIMITATIONS

The process for conducting the test is as follows:

1. Extraction of a blood sample.
2. Extraction of DNA from the biological sample.
3. Massive parallel sequencing of the genetic regions of 543 genes or 248 genes for CGT600 and CGT250, respectively, where known mutations are located. Lists available at http://cgt.igenomix.com/
4. Additional studies: PCR and/or MLPA and Sanger sequencing techniques are used to analyse 6 specific genes in CGT600 (CYP21A2, DMD, F8, FMR1, HBA, and SMN1. Note: DMD and F8 are also analysed by NGS) and 2 specific genes in CGT250 (FMR1 and SMN1). These methods allow us to detect frequent mutations not analysed with NGS technology in the indicated genes. (list available at http://cgt.igenomix.com/).
5. Bioinformatic analysis of the sequencing results (NGS).

To process the sample, the test request form will need to be correctly filled out. If this is not the case, the analysis may be put on hold until the information required has been given to the laboratory.

Given the complexity of the genetic tests and the significant implications of the test results, the results obtained must be interpreted in conjunction with other clinical data, within the general context of a medical practice run by health professionals. The result reports are strictly confidential.

The biological sample –in this case, blood– to be used in the genetic test, will be obtained using standard techniques with little or no risk to the patient's health, and will be analysed by the Igenomix Group ("**Igenomix**"). Nevertheless, Igenomix reserves the right to carry out part or all of the analyses included in the test through Third Party Laboratories certified with recognised international quality standards, or failing this, they will be periodically assessed by Igenomix. Any results obtained in this way will be inspected by Igenomix and this circumstance will be indicated in the final report issued.

The test results will be compared with the genetic profiles of your partner or gamete donor (as applicable), detecting combinations that have a high risk of resulting in offspring developing the disorders and mutations analysed. In the case of gamete donation, the computer system will only provide your doctor with the code of those donors who do not imply a risk for the specific case, without offering any information about the particular genetic profile of any donor.

Although done properly and while there are considerable benefits to the CGT test, limitations exist that are described below:

a. The CGT test only includes the mutations in the list, and no others (list available at http://cgt.igenomix.com/).
b. The massive sequencing technique has the following technical limitations:
    i. DNA changes caused by large rearrangements (deletions and duplications) cannot be detected, except for those included in the list.
    ii. Trinucleotide expansions are not detected, except for those in the list http://cgt.igenomix.com/.
c. A negative result of the CGT test does not rule out:
    i. Onset of genetic disorder due to de novo mutation in one of the parents' gametes cells.
    ii. Presence of somatic or germline mosaicism that creates differences in the DNA between tissues. These types of mosaicism are created after the fusion of parental gametes and can affect a part of, one or several complete tissues. This mosaicism cannot be detected if the tissue where it was created is not studied and also if it is not present in a significant portion of its cells. In any case, the incidence of this happening is relatively low.
    iii. Rare polymorphisms may lead to false negative results.
d. The results of the test may not always provide definitive conclusions with regarding to the reproductive risk. Therefore:
    i. It does not include all existing genetic disorders, since the genetic basis for many of them is still unknown, although the CGT can detect thousands of mutations. It does not include all monogenic diseases whose genetic basis is already known, both for monogenic recessive diseases and X-liked disorders. Some genes included in this test can be associated to dominant phenotypes, however, since this is not a diagnostic test, the genetic counselling will be only provided for recessive and X-linked phenotypes.

ii. Mitochondrial diseases, autosomal dominant diseases, multifactorial diseases or those of digenic inheritance are not included, unless otherwise indicated.

iii. Variants known as variants of uncertain significance (VUS) are not included, since there is not enough clinical information available to classify them as causes of pathologies. Although they could be identified, it is not possible to use this information to obtain a specific clinical recommendation.

iv. There may be other medical reasons that invalidate the test and which should be researched by the doctor before proposing the test, such as the presence of congenital or acquired chimera, temporarily through blood transfusion, or permanently through bone marrow transplant. The congenital chimerism develops when two twin embryos become one; the likelihood of this happening is low or very low. Allogenic bone marrow transplants generate chimera or coexistence of the patient's own cells with others from the donor, including the possibility of an exclusive donor cell colonisation. It is important to consider that these circumstances will lead to discrepant findings if the analysed sample comes from peripheral blood. Scientific literature outlines the possibility of working with a saliva sample to avoid possible discrepancies in genetic findings when it comes to bone marrow transplants.

DATA PRIVACY, STORAGE AND RESEARCH USE OF SAMPLES

Your privacy is a priority for the Igenomix Group ("**Igenomix**"). Your identity and all data referring to your personal information will be confidential and only Igenomix personnel will be permitted access to this information, along with the relevant authorities when required by the laws of the applicable jurisdiction. You will find further information on the Igenomix Privacy Policy, along with all your rights at www.igenomix.com, or this information may be provided to you upon request by sending an email to privacy@igenomix.com.

We would like to inform you that your personal data will only be processed to: (1) Fulfil the obligations arising from the provision of the services contracted by you; (2) Check and guarantee the quality of the services provided (internal audits, quality controls, laboratory validation studies); (3) For educational purposes, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (4) For research purposes, scientific publications and presentations, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (5) Personally address any doubts or suggestions made by the patient during the process and monitor the proper performance and resolution of the test, including the indefinite retention of your data, except where local laws of the applicable jurisdiction state otherwise; and (6) Contact you in the future to request an evaluation of the services received, send commercial communications (including 'cross-selling' and 'upselling') from associated companies, and also to invite you to participate in market research and the development of new products.

You also declare that you understand and accept that you will not obtain, either now or in the future, any economic benefit for any research carried out, and that there is no intention to compensate you for the products developed from any research.

The sample will be analysed by Igenomix or an associated group selected by Igenomix on an international level. Igenomix reserves the right to carry out part or all of the analyses included in the test through Third Party Laboratories certified with recognised international quality standards, or failing this, they will be periodically assessed by Igenomix. Any results obtained in this way will be inspected by Igenomix and this circumstance will be indicated in the final report issued.

Pursuant to the laws on the Protection of Personal Data[1], the requesting party must have the patient's consent to perform the diagnostic tests requested and to process their data. You may, at any time, exercise your rights regarding access, rectification, opposition, erasure, automated decisions, limitation, portability, by sending an email to privacy@igenomix.com, providing proof of the requesting party's identity.

IN RELATION TO THE RESULTS OF MY CGT TEST, I WISH: (INDICATE AN OPTION OF YOUR CHOICE)

☐ Not to receive any information at all: I don't want to have access to or receive any information about the results of the test. However, if the information is necessary to avoid serious damage to my health or that of my biological relatives, information may be given to me or to a legally authorized representative. In any event, the communication will be limited exclusively to the data necessary for such purpose.

☐ To receive the final conclusions: I would like the Igenomix medical team / geneticist to inform me about the final conclusions of the study, accepting that such conclusions might mean the risk of transmitting hereditary diseases under study to my descendants, even though I may not currently show any symptoms of such pathologies.

The result of the **CGT** test will be available and it will be sent to me within a period of no more than 25 business days. A small percentage of samples may be delayed due to unforeseeable causes. Should this occur, the corresponding clinic in charge will be notified.

'The result of the CGT test is limited to the techniques and scientific/medical understanding that are available at the time of testing. The test detects only the mutations that are currently indicated on the website http://cgt.igenomix.com/.'

In any event, I declare that I have received adequate Genetic Counselling from qualified **CENTRE / CLINIC** personnel who have offered me information about the importance of the test, including possible alternatives that I have chosen in view of the results thereof, and who are available to me for any questions or additional genetic counselling that I may require once the results of the **CGT** test are known.

I have been informed that this consent may be withdrawn at any time. However, if such withdrawal takes place once the **CGT** test has been done, **IGENOMIX** may not continue using my genetic data in the computer system, unless it is disassociated from my identity and used for research purposes.

HAVING READ AND UNDERSTOOD THE FOREGOING, I AM AWARE OF:

The indications, procedure, success rate, risks and complications of the proposed treatment, as well as the financial cost of said test(s).

For non-US patients: customers residing outside the United States under certain jurisdictions may at any time request to have their personal information deleted from our active databases, subject to the applicable laws and regulations in each jurisdiction. Although we can delete your personal information from our active databases, part or all of your personal information shall remain stored in back-up files for the purpose of complying with legal, regulatory or other requirements. Information that has already been coded and/or anonymised may not be recoverable or traceable for destruction, deletion or modification. If you wish to have your personal information removed from our active databases, please contact us at privacy@igenomix.com.

The fact that medical staff are at my disposal to expand on any aspect of the information that is not sufficiently clear to me.

I have understood the explanations given to me in clear and simple language, and the doctor who saw me allowed me to make comments, clarifying any issues I raised and informing me that I may freely withdraw my consent at any time.

I am satisfied with the information received and I freely consent to giving a blood sample at the Centre/Clinic which I have attended. I also consent to the sample being sent to Igenomix facilities for the purpose of carrying out the aforementioned test(s).

I also accept that the results of the test(s) may be passed on to my doctor, so that he or she can advise me correspondingly on the suitable treatment to follow.