Fields marked with an asterisk (*) are required.

REQUESTING PHYSICIAN*

Name

Hospital / Clinic / Health center

Tel. no. | Contact email address

Email address to deliver the report

PATIENT INFORMATION (index case)

It is mandatory to include detailed clinical data and family history (appendix). For family testing, fill in one request form and informed consent per studied family member.

Full name / Reference* | Sex*

Date of birth* | MRN* | Ethnicity

Affected*: ○ Yes ○ No Consanguinity*: ○ Yes ○ No

Sample type*: ○ DNA ○ Blood ○ Saliva ○ Mouth swab ○ Tissue ○ Amniotic fluid ○ Chorionic villus sampling

Sample collection date*

Recent blood transfusion (<60 days): ○ Yes ○ No Bone marrow transplant: ○ Yes ○ No

I wish to receive results on secondary and actionable findings identified by genomic analysis (ACMG)[1]: ○ Yes ○ No

[1] Miller et al. Genet Med. 2022 24(7):1407–1414

AUTHORIZED PERSON(S) TO RECEIVE THE RESULTS

In compliance with the Spanish and European personal data protection laws, the results will only be delivered to the persons duly identified in this requisition form.

Name | Surname

E-mail to receive results

Name | Surname

E-mail to receive results

Name | Surname

E-mail to receive results

INVOICING DETAILS

You only have to fill out the billing information if you are not registered as a customer.

○ **Hospital / Institution**
(hospital, clinic, health center)

○ **Self-pay patient**
(patient or representant)
Payment method: ☐ Bank transfer ☐ Credit card

Full name *(institution or particular)* | National ID / Tax number

Address

City | Province / Region / State | Zip code | Country

Contact person | Phone

E-mail to send the invoice*

(*) Only required for institutions/entities

Fields marked with an asterisk (*) are required.

TEST TYPE*

- ○ **Patient testing**
- ○ **Family screening**
  Fill in one test request form per family member. A report will be issued for the index case, and information on relatives will only show inheritance patterns and segregation.
- ○ **Prenatal testing**
  A sample from the mother is required to rule out contamination of fetal samples with maternal cells. Please indicate family and sample information in the form.

REQUESTED ANALYSIS*

NGS gene panel
Consult our list of available panels by clinical area.

Reference

Pathology / Phenotype

02 | Phenotype-based exome analysis

OMIM | Disease / Phenotype / Condition

Consult specific designs by clinical area.

03 | Exome sequencing

WES: ○ Individual ○ Duo ○ Trio EXPRESS CLINICAL EXOME: ○ Individual ○ Duo ○ Trio

Please provide clinical indication, phenotype, HPOs, etc. in the Appendix for this information. The analysis and interpretation are based on and adapted for the clinical indication.

04 | Variant testing

Mutation *(HGVS nomenclature)* | Gene | OMIM

A copy of the original report describing the mutation and a sample from a family member that will be used as a positive control are required.

05 | Single-gene sequencing

Gene | OMIM

Inquire about available genes and the most cost-effective technique for your test.

06 | MLPA targeting a specific gene or region

Gene | OMIM | Region | Methylation

Inquire about available genes and the most cost-effective technique for your test.

07 | Expansions

Gene | OMIM

Inquire about available genes and the most cost-effective technique for your test.

08 | Cytogenetic testing

○ Karyotyping ○ CGH array 60K ○ CGH array 180K

Inquire about sample requirements.

09 | Other types of genetic analysis

OMIM | Gene | Mutation

Inquire about availability and accuracy of testing methods.

*Authorization of the referring physician

I certify that all the information on this request form is correct to the best of my knowledge and that the genetic test indicated below is requested based on my professional judgment and the patient's medical record and family history. I have explained the limitations of this test and answered any health-realted questions the patient had to the best of my ability. If an informed consent form signed by the patient is not attached, I hereby declare that a copy of it is stored in the patient's medical record at the referring facility/hospital. I understand that Health in Code, S.L. may ask for additional clinical and/or family information to ensure correct interpretation of the genetic data in the indicated clinical context, and I accept to share this information if requested.

☐ *By signing this form, I authorize the genetic test for this patient.*

Signature and date

CLINICAL INDICATION*

Please **provide clinical indications and any other clinical information you consider relevant** to this request. You may either directly attach all relevant documents or simply supply it on this page.

This information is **very important for the clinical interpretation of the results.** Missing or incomplete information may lead to misinterpretation of the results in the clinical context, and furthermore, the requested study may not meet the standards stipulated by ISO 15189.

List the main clinical indications for this request. Please include the most relevant clinical findings and attach all relevant medical records and genetic test results related to the clinical indication for the test.

Family and prenatal screening for a mutation previously identified in the family require a copy of the original report describing the variant. Bear in mind that a detailed medical history and information on the genetic profile are essential for accurate test interpretation.

☐ I will send all relevant medical information attached to this request form

FAMILY TREE (if applicable)

Please indicate the index case with an arrow, as well as other relatives included in the study.
Mark affected and healthy individuals according to geneaology standards, as well as any consanguinity.

CAPTURE NGS SEQUENCING PANELS

General panels

- **Global panel of cardiovascular diseases** [406 genes] *Targeted exome sequencing*
  Reference: S-202212924
- **General panel of hereditary heart diseases** [368 genes]
  Reference: S-202313244
- **General panel of cardiomyopathies, arrhythmias and sudden death** [288 genes]
  Reference: S-201906399
- **General panel of cardiomyopathies** [227 genes]
  Reference: S-201906396
- **General panel of arrhythmias and sudden death without structural cardiopathy** [100 genes]
  Reference: S-201906397

Cardiomyopathy

- **Hypertrophic cardiomyopathy (basic panel)** [21 genes]
  Reference: S-201906389
- **Hypertrophic cardiomyopathy (extended panel)** [140 genes]
  Reference: S-201906390
- **Dilated cardiomyopathy - Non-compaction cardiomyopathy** [146 genes]
  Reference: S-201906391
- **Arrhythmogenic cardiomyopathy** [31 genes]
  Reference: S-201906392
- **Restrictive cardiomyopathy** [22 genes]
  Reference: S-201906393

Rare diseases with cardiac affectation

- **RASopathies (Noonan, Costello, LEOPARD)** [27 genes]
  Reference: S-201906395
- **Fabry disease. Sequencing of the *GLA* gene** [1 gene] *NGS Amplicones*
  Reference: S-201601169
- **Familial Amyloidosis. Sequencing of the *TTR* gene** [1 gene] *Sanger*
  Reference: S-201500141
- **Mitochondrial genome sequencing** [37 genes]
  Reference: S-201805389
- **Nuclear mitochondrial genes** [400 genes] *Targeted exome sequencing*
  Reference: S-202008652

Channelopathies and cardiac arrhythmias

- **Long QT syndrome (basic panel)** [11 genes]
  Reference: S-201906402
- **Long QT syndrome (extended panel)** [36 genes]
  Reference: S-201906403
- **Short QT syndrome** [9 genes]
  Reference: S-201906401
- **Catecholaminergic polymorphic ventricular tachycardia** [11 genes]
  Reference: S-201906405
- **Brugada syndrome panel / J Wave syndrome panel** [28 genes]
  Reference: S-201906404
- **Cardiac conduction disease** [54 genes]
  Reference: S-201906449
- **Atrial fibrillation** [55 genes]
  Reference: S-201906450

Aortic, vascular, and connective tissue diseases

- **Aortic and vascular pathologies** [81 genes]
  Reference: S-202313243
- **Ehlers-Danlos syndromes** [47 genes]
  Reference: S-201906569

Congenital cardiopathies and pulmonary hypertension

- **Congenital heart diseases** [114 genes] *Targeted exome sequencing*
  Reference: S-201601108
- **Pulmonary arterial hypertension** [25 genes]
  Reference: S-202007949

INFORMED CONSENT
FOR GENETIC TESTING

The health professional requesting this test undertakes to provide corresponding genetic counseling, with the aim of informing the patient about the purpose of the study, the procedure to be carried out, the limitations and risks, as well as the possible results and the associated implications. They also undertake to resolve any doubt the patient might have before or after the test. In case this is not possible, Health in Code, S.L. provides the necessary genetic counseling upon request.

01 / PURPOSE AND IMPLICATIONS OF THE TEST

I acknowledge the following:

- This genetic test will be done on your biological sample (blood or other tissue), and a written report containing all identified, clinically relevant findings (genetic alterations) related to the indication for the test will be issued. The results of the test may determine that you have or are at an increased risk of developing or transmitting a genetic disorder, or that the identified changes may affect your response to a specific treatment.
- This genetic test may reveal incidental findings that have implications for you and your offspring and/or other members of your family. You must decide if you want to be informed of these findings. In case you do, it is advisable that you also disclose this information to your relatives.
- If you choose not to be informed of incidental findings, your relatives (or their legal guardians) may still be given this information. You can indicate in this form if your relatives wish to be informed about these findings, and this information may be offered on grounds of medical ethics, if the treating physician decides that these findings would represent a severe health risk to them. Shared information will be limited to what is proportionate and necessary.
- Sometimes, a genetic test on samples from other relatives is necessary for a correct interpretation of the results. Results may be affected by family relationship, and genetic testing may reveal previously unknown family relationships (eg, non-biological paternity).

02 / RESULTS OF THE GENETIC TEST

I understand that the genetic test can have four possible results:

- **Positive result:** One or more genetic variants (pathogenic or possibly pathogenic) considered to be the underlying reason for the diagnostic suspicion are identified.
- **Negative result:** No genetic variant with clinical implications is identified. A negative result does not fully rule out the presence of a genetic disorder or predisposition to disease development. Some genetic disorders have multiple causes, and it is not possible to test for all of them. A negative result may occur due to scientific, knowledge, and/or technological limitations.
- **Inconclusive result*** ***(*not applicable for direct mutation analysis):*** One or more genetic variants of unknown clinical significance (VUS) are identified. These variants cannot be used to make medical decisions for the patient and/or the patient's family members. In some cases, you or other members of your family may be recommended additional testing, in order to reassess the clinical significance of these variants. Only variants of uncertain significance that are considered clinically relevant by the clinical team will appear in the report.
- **Non-informative result:** Results were not obtained. This can occasionally occur due to technical failure, poor quality/insufficient quantity of the sample, or sample contamination. If needed, a new sample may be requested.

The identified genetic variants are classified into five pathogenicity categories according to the American College of Medical Genetics and Genomics (ACMG) standards (Richards et al., Genet Med, 2015, 17(5): 405-424). Genetic variants can be reclassified over time as new scientific evidence and clinical data are acquired, or the condition of the patient changes. As certain cases may benefit from these new discoveries, it is sometimes recommended that the collected data be re-examined after a certain period of time, for instance yearly.

As recommended by the American College of Medical Genetics and Genomics (ACMG), exome-based studies, in addition to the main reason for testing, can screen for pathogenic (or probably pathogenic) genetic variants in certain disease-associated genes that are considered to be clinically actionable, that is, for diseases with already established prevention strategies or treatments. These genes have been associated with a predisposition to certain types of cancer, cardiovascular diseases, and inborn errors of metabolism, among others. (https://www.ncbi.nlm.nih.gov/clinvar/docs/acmg/)

Secondary findings will only be reported if the patient has explicitly stated in the informed consent that they wish to be informed about them.

I give my consent (for me and/or my relatives) to be informed about secondary findings (ACMG):

○ Yes ○ No

In the case of genomic studies (eg, exome sequencing or gene panels), there is a chance that the test detects unanticipated findings (incidental or unsolicited findings) that may have an impact on your health, but that are not related to the symptoms of your disease or the reason why the study was requested.

Incidental findings are generally not reported, but may be relayed to your doctor if they have a potential medical implication and added to the report if deemed necessary.

03 / LIMITATIONS AND RISKS

I understand that:

- Some genetic tests are done on a blood sample and that the blood extraction technique can temporarily cause small bleeding and pain at the puncture site, dizziness, loss of consciousness, or bruising that may appear during the following days.
- Communication of the results of the genetic test may result in psychological stress for the patient and/or other family members.
- There are various types of genetic alterations and that no technique is capable of detecting all of them. Each technique has its limitations, which will be duly indicated in the final report.
- Exceptionally, the result of the genetic study may be inaccurate due to errors in the collection, labeling, or processing of the sample or in the analysis/interpretation of data.
- The analysis and clinical interpretation of the genetic study is done with currently available knowledge and technologies. As scientific knowledge advances, new scientific evidence may add to or change the analysis and interpretation of the study.

- Patient data can be re-analyzed and that the study applicant or patient may be contacted again in the future if new findings associated with the reason for the test are identified.
- Re-analysis of obtained results is not routinely performed in our laboratory, but it can be done in some genetic studies (eg, clinical exome sequencing) upon request and that issuing a new report would incur additional expenses.

04 / GENETIC COUNSELING

It must be borne in mind that the result of the genetic test may not be used as a substitute for medical diagnosis or genetic counseling and that they must be communicated and interpreted by a health professional. Health in Code, S.L. is not responsible for any damages or harm that may arise from the use of the study data by the patient, the physician, or third parties.

It must also be borne in mind that the final report will be sent to the applicant within the turnaroud time specified in our service catalog, although, occasionally, unforeseen circumstances may cause a delay in the delivery of the results, about which case they would be duly informed.

The patient has been informed about the nature and the purpose of this genetic test, the procedure, its limitations, and the possible results and implications. They have understood the information they were provided and all their questions have been answered to their satisfaction.

Health in Code, S.L will gladly help the health professional or the patient with any question they may have regarding the genetic study.

Health in Code, S.L may contact you, only if necessary, to request additional clinical data.

05 / PRIVACY, DATA PROTECTION, DATA STORAGE (SAMPLES), AND RESEARCH

Your sample and your data will be shared with Health in Code S.L., a company with a level of data protection that is compliant with national and European legislation, in order carry out the indicated genetic study. Always in line with ethical considerations and current regulations, Health in Code S.L. may in turn, for the purposes of the study, share said information with other designated centers, which comply with the same regulations.

In accordance with the provisions of the Genreral Data Protection Regulation (2016/679 "GDPR") and with Organic Law 3/2018, of December 5, on Personal Data Protection and Guarantee of Digital Rights, your personal data will be used for our relationship and to provide the requested service, allowing us to process your personal data within the law. Likewise, your personal data may be used for: any questions that you or the requesting physician may have for the management or follow-up of the case; quality procedures; and for future contact with you should new, useful clinical evidence arise.

Genetic data collected may be utilized for research purposes in order to further scientific understanding and presented through scientific publications or included in genomic databases, unless explicitly refused by the patient. Research conducted on genetic data provides new evidence for variant reclassification, resulting in a higher level of accuracy when interpreting genetic test results. This, in turn, helps better diagnose genetic diseases and implement effective preventive and therapeutic measures.

☐ *I do not grant permission to use the collected data for research, variant reclassification, or improvement of diagnostic processes.*

Although the data are anonymized whenever they are shared with the scientific community, the risk of re-identification cannot be completely ruled out due to the uniqueness of genetic information. The risk of this occuring is currently very low. It is also possible for someone to gain unauthorized access or break into the system that stores the information. Every precaution is being taken to minimize this risk, but it is not possible to anticipate or eliminate all privacy risks.

You will not receive any financial benefit from any research discoveries or product development.

Only employees with proper authorization will have access to your personal data. Likewise, Health in Code, S.L. reserves the right for part or all of the genetic study to be done in duly accredited third-party laboratories, which may have knowledge of your personal data for the provision of services. Similarly, your information will be shared with public or private entities we are obliged by law to share data with.

We will keep store your personal data for the duration of our relationship and, subsequently, for the period determined by law. At any time, you can contact us to request information about the personal data we have stored about you, rectify them if they are incorrect, and delete them once our relationship has ended, if it is legally possible. You also have the right to data portability, in other words, transfer of your personal data from one service to another.

If you want to exercise any of these rights, please send a written request to our address at HEALTH IN CODE, S.L, C/ DE LA TRAVESÍA, S/N, EDIFICIO BIOHUB 15E BASE 5 – 46224 VALENCIA, SPAIN, attaching a copy of your ID for your identification.

REQUESTED GENETIC TESTING

Please, specify the requested genetic test (required)

Reference (optional)

*** Patient (or parent/legal guardian) signature**

I hereby declare that by signing this request form, I voluntarily authorize Health in Code, S.L. to perform the genetic test specified below. Likewise, I have been adequately informed regarding the risks, benefits, and limitations of this genetic test.

If the patient is a minor, I, the undersigned, in my capacity as ○ **parent** or ○ **legal guardian**, authorize the indicated genetic test. I represent that I am the only legal guardian of this child, or that the other parent is aware and does not oppose this request.

Full name | ID no.

Signature and date

You may withdraw this consent at any time by notifying Health in Code, S.L. in writing.