The fields marked with (*) are required to carry out the genetic test.

REQUESTING PHYSICIAN *

Name

Hospital / Clinic / Center

Tel. no. | Contact email

Email address for the report

PATIENT DETAILS (index case)

It is mandatory to include details about the patient's clinical indication and family history (appendix). For family testing, use separate request and informed consent forms for each person.

Full name / Reference * | Sex *

Date of birth * | MRN * | Ethnicity

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

Type of sample *: ○ DNA ○ Blood ○ Saliva ○ Buccal swab ○ Tissue ○ Amniotic fluid ○ Chorionic villus sampling

*For DNA, please specify its origin **:

Sample extraction date *

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

In the case of genomic testing, would you like to be notified of secondary and actionable findings (ACMG)?[1] ○ Yes ○ No

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

PEOPLE AUTHORIZED TO RECEIVE THE REPORT

In compliance with Spanish and European data protection legislation, the results shall only be sent to those people identified in the request form.

First name | Surname(s)

Email address for the report

First name | Surname(s)

Email address for the report

First name | Surname(s)

Email address for the report

BILLING INFORMATION

Only fill in the billing information if you are not registered as a customer.

○ **Institution / Entity**
(hospital, clinic, or health center)

○ **Individual**
(patient or representative)

Payment methods: ☐ Bank transfer ☐ Credit card

Name *(institution or individual)* | Tax code / ID no.

Address

City | Province/Region | Post Code | Country

Contact person | Contact phone no.

Email address for the bill *

(*) Only required for institutions/entities

The fields marked with (*) are required to carry out the genetic test.

TYPE OF TEST *

- ○ Individual testing
- ○ Family screening
  Use separate request and informed consent forms for each member of the family. The results report will relate to the index case and will include genetic information on family members only as a reference for inheritance and segregation patterns.
- ○ Prenatal testing
  A sample from the mother is required to rule out maternal contamination of the fetal sample. Please indicate family and sample information on the form.

TEST REQUESTED *

Please remember to sign the request form on the following page to authorize the genetic test for the patient.

01 GENOME SEQUENCING

CLINICAL GENOME TESTING
Sequencing + Report with clinical/diagnostic guidance

○ Individual ○ Duo ○ Trio

Describe the clinical indication, phenotype, HPOs, etc. on the appendix page designed for this purpose. The analysis and interpretation is carried out in line with the clinical indication provided.

Do you require access to Emedgene?* ○ Yes ○ No

WHOLE GENOME SEQUENCING
WGS wet lab + Raw Data

○ 100Gb 30X ○ 200Gb 60X

Do you require access to Emedgene?* ○ Yes ○ No

02 NGS GENE PANEL

See our list of available panels per clinical specialty.

If you know the reference for the panel you require, please enter it below:

Pathology / Phenotype *

03 PHENOTYPE-BASED EXOME ANALYSIS

See specific designs per clinical specialty.

If you know the reference for the test you require, please enter it below:

OMIM

Disease, phenotype or condition *

04 EXOME SEQUENCING

WHOLE EXOME

○ Individual ○ Duo ○ Trio

Describe the clinical indication, phenotype, HPOs, etc. on the appendix page designed for this purpose. The analysis and interpretation is carried out in line with the clinical indication provided.

EXPRESS CLINICAL EXOME

○ Individual ○ Duo ○ Trio

Describe the clinical indication, phenotype, HPOs, etc. on the appendix page designed for this purpose. The analysis and interpretation is carried out in line with the clinical indication provided.

[1/2] Continue >

[2/2] **Continue** ›

The fields marked with (*) are required to carry out the genetic test.

05 ANALYSIS OF SPECIFIC GENETIC VARIANT

A copy of the original report describing the mutation is required, in addition to a sample from a family member as a positive control.

Mutation *(HGVS nomenclature)* | Gene | OMIM

Is interpretation of the variant required? * ○ Yes ○ No

If yes, and the index case has been analyzed at Health in Code, indicate this below.

Index case ⓘ

ⓘ *You may enter the "HIC sample number", "Medical Record Number" or any other information that may help us identify the index case, such as the patient's full name.*

06 SINGLE-GENE SEQUENCING

Check availability of genes and the most cost-effective technology for their analysis.

Gene | OMIM

07 MLPA OF A GENE OR REGION

Check availability of genes and the most cost-effective technology for their analysis.

Gene | OMIM | Region | Methylation

08 EXPANSIONS

Check availability of genes and the most cost-effective technology for their analysis.

Gene | OMIM

09 CYTOGENETIC TESTING

Check sample requirements.

○ Karyotype ○ 60K array CGH ○ 180K array CGH

10 OTHER TYPES OF GENETIC TESTING

Check availability and precision of the testing.

OMIM | Gene | Mutation

*Authorization from requesting physician

I certify that the information provided in this form is accurate to the best of my knowledge and that I have requested the indicated genetic test based on my professional judgment and the patient's medical and family history. I have explained the limitations of this study and have answered all the patient's medical-related questions. If the patient has not provided a signed copy of the informed consent form, I certify that there is a copy in the patient's medical records at my clinic. I understand that Health in Code, S.L. may require additional medical and family information to correctly interpret the data obtained within the indicated clinical context and I agree to provide this information if necessary.

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

Date and signature

CLINICAL INDICATION*

Please provide the **clinical indication for this test and any medical information** that may be relevant, either by attaching it or using this page of the form.

This information is **very important to correctly interpret the results from a medical perspective**. Missing or incomplete information may prevent accurate interpretation within a clinical context. The test may also fall outside of the ISO 15189 accreditation scope.

Please list the main clinical indication for this test, including the most relevant clinical findings for the patient, and provide all the medical information and genetic reports related to the clinical indication for the test.

In the case of family screening and prenatal testing for a mutation previously identified within the family, we will require a copy of the original report detailing the variant in question. It is vital that we have detailed medical information and that the genetic variants in question are identified to provide a precise interpretation of the test.

☐ Medical information attached to this form

FAMILY HISTORY (if applicable)

Indicate the index case with an arrow, as well as the family members to be included in the test.

Mark affected and healthy individuals as per genealogy standards, as well as any consanguinity.

CAPTURE NGS SEQUENCING PANELS

General panels

- **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 the required genetic counseling to the patient regarding the purpose of the test, the procedure to be carried out, the limitations and risks, and the potential findings and implications. They also commit to resolve any queries before and after the genetic test is carried out. Should this not be possible, Health in Code, S.L. may provide the necessary genetic counseling upon request.

01 / PURPOSE OF THE STUDY AND IMPLICATIONS

You acknowledge the following:

- A genetic test shall be performed on a biological sample provided by yourself (blood or other tissue) and a written report shall be issued with any clinically relevant findings (genetic disorders) related to the purpose of the test. The results of the genetic test may determine that you have an increased risk of suffering from or transmitting a genetic disorder, and may affect how you respond to a specific treatment.
- The results of this genetic test may have implications for yourself, your offspring and other members of your family. If this is the case, it is advisable that you inform your family members of the findings yourself.
- You have the right to not be informed of the results of this genetic test. If you choose to not be informed of the results, we may inform your family members (or legal guardians) if you give your consent and/or there are medically ethical grounds to do so, should this information be necessary to avoid serious harm to their health, as determined by the treating physician. Communication shall be limited exclusively to the information required for these purposes.
- At times, for certain genetic tests, we may also require samples from family members to interpret the results correctly. In these cases, the results may reveal parental relations that were previously unknown (e.g., non-biological paternity).
- In the case of pharmacogenetic testing, bear in mind that it is designed for instructive, informational and research purposes based on the available scientific evidence. As such, its objective is to inform you about contributing factors for the treatment of certain disorders and diseases. The information that is obtained through pharmacogenetic testing is not intended to diagnose any disorders or diseases, and under no circumstances may it be used in place of specialist care provided by healthcare professionals.

02 / RESULTS OF THE GENETIC TEST

You understand that the genetic test may return four different types of results:

- **Positive result:** One or more genetic variants (pathogenic or possibly pathogenic) have been identified that are believed to be the cause of the suspected diagnosis or the clinical indication that led to the test.
- **Negative result:** No genetic variant with clinical implications has been identified. A negative result does not necessarily rule out the possibility of a genetic disorder or predisposition to a disease. Some genetic disorders have many different causes and it is not always possible to test for all of them. A negative result could also occur as a result of scientific, technical and/or knowledge-based limitations.
- **Non-conclusive result:** One or more genetic variants have been identified but we do not know how relevant they are yet. These are known as "variants of unknown significance", or VUSes. These variants cannot be used as the basis for medical decisions. In certain cases, additional testing may be recommended for yourself or for other members of your family to reassess the clinical significance of these variants. The report will only include variants of unknown significance if they are considered clinically relevant by the clinical team.
- **Non-informative result:** No results have been obtained. This may occasionally happen as a result of a technical fault caused by an issue related to sample quality/quantity or sample contamination. In this case a new sample may be requested.

The identified genetic variants are classified into five different categories of pathogenicity, as per the ACMG standards (American College of Medical Genetics and Genomics; Richards et al. *Genet Med* 2015 17(5):405-424). Classification of genetic variants may change over time as a result of rapid advances in scientific knowledge and available clinical evidence, or due to changes in the patient's condition. For this reason, we may occasionally recommend a reanalysis of the data obtained after a certain time.

With exome and genome testing, as recommended by the ACMG, in addition to the primary purpose of the test, we may also analyze pathogenic (or possibly pathogenic) genetic variants from a list of genes associated with diseases that are considered clinically actionable, or in other words, diseases that can be prevented or treated. The genes or regions included in this list are associated with a predisposition to certain types of cancer, cardiovascular disease and metabolic disorders, among others. (https://www.ncbi.nlm.nih.gov/clinvar/docs/acmg/)

Findings in these genes are known as secondary findings and you will only be informed of them should you have explicitly stated in the informed consent form that you would like to be made aware of them.

I hereby give my consent to be informed about secondary findings (ACMG):

○ Yes ○ No

With genomic testing (e.g., genome, exome, or panels with a high number of genes), it is possible to detect incidental findings (findings that were not requested) that could have potential implications for your health but are not related to the symptoms of the disease or the clinical indication that led to the test. You will not be routinely informed of these incidental findings, but they may be provided to your doctor should they have

significant clinical implications. You will only be informed of these findings should you have explicitly stated in the informed consent form that you would like to be made aware of them.

I hereby give my consent to be informed (and/or for my family members to be informed) of any incidental findings (ACMG):

○ Yes ○ No

03 / LIMITATIONS AND RISKS

You acknowledge the following:

- If the genetic test is performed using a blood sample, the blood extraction method may cause temporary and minimal bleeding and pain around the puncture site, in addition to dizziness or fainting, and bruising may appear over the following days.
- Upon receiving the results of the genetic test, the patient and/or other family members may suffer from psychological stress.
- There are various types of genetic disorders and no technique is capable of detecting all of them. Every technique has its own specific limitations, which will be duly indicated in the results report.
- In exceptional circumstances, the genetic test may return inaccurate results due to errors when taking, labeling, or processing the sample, or when analyzing/interpreting the data.
- The analysis and clinical interpretation of the genetic test is performed using the knowledge and technology that is currently available to us. As our scientific knowledge expands, the analysis and interpretation of the test may change or be supplemented.
- The data may be reanalyzed and the patient or the party requesting the test may be contacted again in the future should new findings be made related to the clinical indication behind the test.
- The data obtained in the test is not routinely reanalyzed at our laboratory, but it is possible for certain genetic tests (e.g., clinical exome or genome testing) upon request, with additional fees required to issue a new results report.

Limitations of genome sequencing

This test cannot sequence a person's entire genome nor can it fully identify every single possible genetic condition. Genome testing will provide information about a wide array of genetic changes. However, the patient will not be informed about the majority of changes detected as there will likely not be enough information about their clinical relevance. They will only be informed about genetic changes that have the potential to trigger a condition related to their clinical condition. That being said, we cannot predict how serious the condition will be nor at what age the patient may develop symptoms. The genetic differences may not explain the medical condition in question and they may not lead to any change in the current therapeutic and/or pharmacological treatment or approach.

04 / GENETIC COUNSELING

You understand that the genetic test results report is not a substitute for a medical diagnosis or genetic counseling, and that the results should be explained and interpreted by a healthcare professional. Health in Code, S.L. is not responsible for any harmful consequences that may arise from the use of the test data by yourself, the requesting party or any third parties.

You understand that the results report shall be provided to the party that requested the test within the timescale indicated in our service catalog. There may occasionally be delays in delivering the results due to unforeseen problems. If this does happen, the requesting party shall be duly notified.

You have been informed about the purpose of the test, the procedure to be carried out, the limitations of the test, and the potential results and implications. You understand the information you have been given and any queries that you had have been successfully resolved.

Health in Code, S.L is available to answer any questions the patient or healthcare professional may have regarding the genetic testing.

You understand that the team at Health in Code, S.L. may contact you if necessary to request further clinical information.

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

To perform the indicated genetic test, your sample and data will be shared with Health in Code S.L., a company with data protection infrastructure that is compliant with Spanish and European legislation. To complete the testing effectively, Health in Code S.L. may share said information with other designated centers, which also comply with the same legislation, in accordance with ethical considerations and current regulations.

In accordance with the provisions of the European General Data Protection Regulation 2016/679 (GDPR) and Spanish Organic Law 3/2018 of December 5 on the Protection of Personal Data and Guarantee of Digital Rights, your personal data will be used to maintain our relationship and to provide you with the requested service, which serves as the lawful basis for us to process said personal data. This personal data may be used to respond to and follow up on any queries that you or the requesting party may have, and it may also be used for quality procedures or for contacting you in the future to update relevant clinical information.

The genetic data obtained may be used for research purposes to expand scientific knowledge in scientific publications or genomic databases, unless you explicitly oppose such use. These research activities provide new evidence for reclassifying variants, thus enabling more precise interpretation of results and enhancing diagnosis, prevention and treatment of genetic diseases.

☐ *I do not authorize the use of my data for research purposes or for reclassifying variants and updating and enhancing diagnostic processes.*

Although the data shared with the scientific community is anonymous, the risk of identification cannot be entirely excluded due to the unique nature of genetic information. However, the risk of this occurring is very low. It is also possible for someone to break into or gain unauthorized access to the system storing the data, although all appropriate measures shall be taken to minimize this risk. We also cannot entirely exclude other privacy risks that may not have yet been foreseen.

You understand that you will not receive any financial benefit from research carried out or products developed.

Only duly authorized personnel from our organization will have access to your personal data. Furthermore, Health in Code, S.L. reserves the right to perform part of or the entirety of the genetic testing at duly accredited third-party laboratories, which will have access to your personal data to provide the requested services. Your data may also be made available to private or public entities should we be obliged to provide them with your personal data in order to comply with certain laws.

We shall store your personal data throughout our relationship, and beyond, for the time period stipulated by the law. You may contact us at any time to find out what data we have on you, correct said data if it is inaccurate, and request its erasure once our relationship has come to an end, should this be legally possible. You also have the right to request the transfer of your data to another entity (portability).

To exercise any of these rights, send a request in writing to the following address, with a copy of your ID so we can identify you: HEALTH IN CODE, S.L whose address is C/ TRAVESSIA, 15E BASE 5, EDIFICIO BIOHUB – MARINA DE VALENCIA, 46024 VALENCIA, SPAIN.

GENETIC TEST REQUESTED

Specify the requested genetic test (compulsory)

Reference (optional)

* Signature of patient, mother, father, or legal guardian

By signing this document, I voluntarily authorize Health in Code, S.L. to perform the indicated genetic test. I have been adequately informed of the risks, benefits, and limitations of this genetic test.

In the case of a minor or a person without legal capacity, as ○ **mother**, ○ **father**, ○ **legal guardian**, I authorize this genetic test. I confirm that the signatory is the sole legal guardian and that the other parent does not oppose this test being performed on our child.

Name and surname(s) | ID number

Date and signature

Your informed consent may be revoked at any time by notifying Health in Code, S.L. in writing.