UniversitätsKlinikum Heidelberg

Institute of Human Genetics
Im Neuenheimer Feld 366
69120 Heidelberg
Germany

Prof. Dr. med. C. Schaaf
Medical Director

Laboratory for Molecular Genetic Diagnostics
Head: Dr. rer. nat. K. Hinderhofer
phone: 06221-56-39568

For general information call our Diagnostic Results Office
phone: 06221-56-32484/ Fax: 06221-56-5091
e-mail: humangen.diagnostik@med.uni-heidelberg.de

DAkkS Deutsche Akkreditierungsstelle D-ML-13060-03-00

Request Form Molecular Genetics

Enclosed sample of: female ☐ male ☐ **Date of sample collection:** **Family name:** **First name:** **Date of birth.:** **Address:** **Ethnical Origin**	**Sender´s name and direction:** Hospital / Ward / Out-patients´ Department / Name of Physician (stamp) Phone no.: Fax no:

Coverage of costs:	☐ Public Health / Outpatient (with referral letter)	☐ Public Health Insurance/ Inpatient	☐ Private Health Insurance/ Outpatient	☐ Private Health Insurance/ Inpatient	☐Self-paying patient

For self-paying patients / Patients insured in a Public Health Insurance scheme without referral letter:
I am aware, that all costs will have to be covered by myself and I explicitly declare that I assume full responsibility for all costs associated with all necessary servicing. Date: Signature:

Patient Information

Indication: If applicable, pedigree // Description of symptoms // Details on pregnancy (week of gestation) // If applicable, copies of previous reports

Additional information:

☐ if molecular genetic testing has already been carried out in the family:

Family name or name of the index patient: _____

When and where? _____ (in case of external analysis report must be attached)

☐ Samples of other family members: ☐ have been dispatched: ☐ will follow:

Family name, First name,	Date of birth	Degree of kinship	Affected?
_____	_____	*mother*	_____
_____	_____	*father*	_____
_____	_____	*further child(ren)*	_____

Name of responsible physician:.....**Phone no:**.....
(block letters)

.....
Date and signature of responsible physician

See next pages for request **Please fill in informed consent enclosed!**

Informed consent for genetic testing (according to GenDG)

Dear patient,
In order to evaluate or clarify the diagnosis specified below, it is considered to perform molecular genetic testing on you / your child. According to the German Genetic Diagnosis Act (GenDG) prior to any genetic analysis detailed medical information is required. Generally, written informed consent has to be obtained from every patient.
For your information please read the following and mark the appropriate answers.

Name: .....

Date of birth: .....

Address: .....

.....

Molecular genetic testing examines the genetic material (DNA) with respect to genetic alterations which could be causative for the disease / disorder that has occurred or has been suspected in you or any of your family members. In case of a suspected diagnosis for a particular disease, the respective gene / genes will be examined. If the clinical diagnosis cannot be restricted to a particular disorder, many different genetic variants will be analysed and detected simultaneously (e.g. by microarray analysis), so as to obtain a genome wide overview.

In case a disease-causing genetic variant (e.g. mutation) is detected, the diagnosis can generally be considered very reliable. If no genetic variation (mutation) can be identified as the cause of your disease, there is still a possibility of a causative mutation in the examined gene / genes or in one or several other genes. Hence, a genetic disease or predisposition to a disorder generally cannot be fully excluded. In such case, we will try to estimate the probability for you or your relatives to be at risk of developing a disease i.e. of being predisposed to a particular genetic condition. Occasionally, the clinical relevance of detected genetic variations remains uncertain. In this case, it will be mentioned in the diagnosis and be discussed with you. Unfortunately, it is not possible to provide detailed information about all genetic variations that may be mainly or to some extent causative for your disease as well as to exclude every single risk for you or your relatives (especially for your children) by means of a genetic analysis. In case that several family members wish to undergo genetic testing it is absolutely essential for us to know the true biological relationship between the individual family members for correct interpretation of the diagnosis. Should the interpretation of a genetic analysis lead to doubts regarding the accuracy of the provided information about the kinship, this will not be disclosed to you unless it is relevant in counselling for the reason for which the sample was submitted.

Please note that there is an inherent minimal risk of confusion when handling samples and performing a laboratory analysis, which can never be completely excluded. However, all precautions are taken to avoid this or other mistakes.

Please read the following carefully and confirm your consent by signing below:

My physician has informed me about the significance and consequences of the genetic examination mentioned below and has given me adequate time to think my decision over. I understand that I can withdraw my consent at any time.

With my signature I consent to the genetic tests for me / my child and the sampling of blood or tissue necessary to clarify the specified diagnosis:

.....

In the context of chromosome microarray testing, next generation sequencing gene panel testing or exome sequencing, genetic variants may be detected that are not related to the primary indication for testing, but which may be relevant and medically actionable for other disorders. These are considered “secondary findings” (see the explanations in our patient information sheet). I would like to be informed about secondary findings.	❒ yes ❒ no
I consent to the data / results collected about the disease in question being used in encrypted form for scientific purposes and published anonymously in specialist journals.	❒ yes ❒ no
According to the German Genetic Diagnosis Act (GenDG) any sample material must be destroyed after completion of the genetic test. Only with your expressed consent, it may be stored longer. Surplus sample material may be required to verify some results (follow-up testing), as well as for necessary quality controls. I consent to my sample being stored for follow-up testing, for future new diagnostic possibilities with regard to the above mentioned medical question / problem, and for quality controls.	❒ yes ❒ no
Surplus material may be an important source for further research and development in the field of medical genetic diagnostics. However, before such use, samples will be anonymised and coded in a way which makes it impossible for any other party to track the sample back to an individual. I consent to my coded sample being stored and used in future research.	❒ yes ❒ no
According to the German Genetic Diagnosis Act (GenDG) any family data on you / your child and any genetic data must be destroyed after 10 years. However, these results may later on become important for your children or grandchildren. I consent to my family data / test results / data of my child being stored beyond this period foreseen by law to enable future testing or counseling of my family members.	❒ yes ❒ no

.....

Date, Place **Signature of the patient / of the legal representative**

Please tick appropriate box(es)

☐ **Storage of DNA specimen** (requires the appropriate consent, otherwise the material will be destroyed after one month)

☐ **Chromosome microarray analysis** (genome wide screening for deletions and duplications)
- ☐ incl. chromosome analysis

We recommend performing a conventional chromosome analysis prior to chromosome microarray analysis (CMA). German health insurance currently requires traditional chromosome analysis as a prerequisite for CMA analysis. If this has not been done yet, please send us an additional NH4 heparin blood sample for chromosome analysis. If possible, please enclose a medical report from your medical geneticist or pediatrician.

☐ **Exome wide analysis based on single whole genome sequencing** [#] ► blood samples of the patient **and** his parents are required. Please provide detailed medical reference information including the main disease symptoms and/or HPO terms (https://hpo.jax.org/app/) and, if possible, a current medical report.

☐ **Exome wide analysis based on trio whole genome sequencing** [#] ► blood samples of the patient **and** his parents are required. Please provide detailed medical reference information including the main disease symptoms and/or HPO terms (https://hpo.jax.org/app/) and, if possible, a current medical report.

☐ **Preimplantation genetic diagnosis (PGD) ►announcement required**
- ☐ Identification of family-specific polymorphic markers linked to the disease-related gene
- ☐ Testing of the established family-specific (likely) pathogenic variant detection strategy on single cells (leucocytes)

Neuropediatric and other disorders:

☐ Angelman syndrome
- ☐ incl. chromosome analysis

☐ Azoospermia (AZF) [#]
- ☐ incl. chromosome analysis

☐ Cystic fibrosis (CF) (*CFTR* gene)
Ethnic origin of the patient_____ (important for risk calculation)

☐ CBAVD (CAVD) diagnostics (atypical CF, male infertility) (*CFTR* gene)
Ethnic origin of the patient_____ (important for risk calculation)
- ☐ incl. chromosome analysis

☐ DMD/BMD Muscular dystrophy type Duchenne or type Becker (DMD gene)

☐ Fragile X syndrome (*FMR1* gene)
- ☐ incl. chromosome analysis

☐ Hereditary amyloidosis
- ☐ Transthyretin (*TTR* gene)
- ☐ Apolipoprotein A-I (*APOA1* gene)
- ☐ Fibrinogen alpha (*FGA* gene)

☐ Huntington´s disease (number of repeats in the *HTT* gene)
- ☐ test of symptomatic individual
- ☐ presymptomatic test (genetic counseling mandatory prior to testing)

☐ Leri-Weill syndrome / short stature (*SHOX* gene) [#]

☐ Pelizaeus-Merzbacher disease (*PLP1* gene) [#]

☐ Prader-Willi / Angelman disease
- ☐ incl. chromosome analysis

☐ Pulmonary arterial hypertension (PAH)[1] / Osler-Rendu-Weber syndrome (HHT; Hereditary hemorrhagic telangiectasia)[2] / Pulmonary Veno-Occlusive Disease (PVOD)[3] (MGPS)
- ☐ Core genes: *BMPR2*-[1,2], *ACVRL1(ALK1)*-[1,2], *EIF2AK4*-[1,3], *ENG* gene[1,2] incl. MLPA (*BMPR2-*, *ACVRL1(ALK1-)*, *ENG* gene)
- ☐ Additional genes: *ABCC8*-[1], *AQP1*-[1], *ATPA13A3*-[1], *BMPR1B*-[1], *CAV-1*[1], *GDF2 (BMP9)*-[1,2], *KCNA5*-[1], *KCNK3*-[1], *KDR*-[1], *KLF2*-[1], *SMAD4*[1,2-], *SMAD9*-[1], *SOX17*-[1], *TBX4* gene[1]

☐ Rett-syndrome (*MECP2* gene)

☐ Spinal muscular atrophy (SMA) (copy numbers exon 7 of the *SMN1* and *SMN2* gene)

☐ Uniparental disomy / Microsatellite ► blood samples of the patient **and** his parents are required
- ☐ UPD chromosome 7
- ☐ UPD chromosome 14
- ☐ UPD chromosome 15
- ☐ UPD chromosome X

Pharmacogenetics:

☐ Testing for following clinically relevant variants in *DPYD* gene due to (planned) 5-fluorouracil-based therapy: c.1679T>G (*13), c.1905+1G>A (*2A, exon 14-skipping), c.1236G>A (HapB3), c.2846A>T*)* [#]

[#]: non accredited analysis

Neurotransmitter disorders and Pterin metabolism defects:

☐ Tyrosin hydroxylase deficiency *(TH* gene*)* #
☐ Aromatic L-amino acid decarboxylase deficiency *(DDC* gene*)* #
☐ 6 Pyruvoyl-tetrahydropterin synthetase deficiency (BH_4-deficiency) *(PTS* gene*)* #
☐ Dihydropteridin reductase deficiency (BH_4-deficiency) *(QDPR* gene*)* #
☐ GTP cyclohydrolase I deficiency (BH_4-deficiency) *(GCH1* gene*)* #
☐ Sepiapterin reductase deficiency (BH_4-deficiency) *(SPR* gene*)* #

Metabolic disorders:

☐ Congenital adrenal hyperplasia (21-Hydroxylase deficiency; CAH) (*CYP21A2* gene)
☐ Glutaric aciduria type I (*GCDH* gene)
☐ Homocystinuria (*CBS* gene) #
☐ LCHAD deficiency (*HADHA* gene) #
☐ MCAD deficiency (*ACADM* gene)
☐ Ornithine transcarbamylase deficiency (*OTC* gene)
☐ Phenylketonuria/Hyperphenylalaninemia (*PAH* gene)
☐ Hyperphenylalaninemia (*DNAJC12* gene) #
☐ Smith-Lemli-Opitz syndrome (*DHCR7* gene)
☐ Methylmalonic aciduria (*MUT* gene) #
☐ Methylglutaconic aciduria type 1 (*AUH* gene) #
☐ Fabry disease (*GLA* gene) #
☐ Phosphoenolpyruvate carboxykinase deficiency, cytosolic (*PCK1* gene) #

Hereditary tumor syndromes:

In case of predictive testing/ variant screening, please enclose a copy of original report.

Autosomal recessive adenomatous polyposis (MAP)
- ☐ complete variant screening analysis in the *MUTYH* gene

Familial adenomatous polyposis (FAP)
- ☐ complete variant screening in the *APC* gene incl. MLPA
- ☐ test for familial (likely) pathogenic variant (please enclose copy of original report)

Familial breast- and ovarian cancer (MGPS)
- ☐ complete variant screening in the *BRCA1, BRCA2, RAD51C, RAD51D, CHEK2, PALB2, ATM, BRIP1, BARD1, CDH1,* and *TP53 gene,* incl. MLPA (*BRCA1* and *BRCA2* gene)
- ☐ complete variant screening in the *BRCA1, BRCA2, RAD51C, RAD51D, CHEK2, PALB2, ATM, BRIP1, BARD1,* and *CDH1 gene,* incl. MLPA (*BRCA1* and *BRCA2* gene)
- ☐ complete variant screening in the *BRCA1* and *BRCA2* gene, incl. MLPA (*BRCA1* and *BRCA2* gene)
- ☐ additional genes associated with ovarian/colorectal cancer: *MLH1*, *MSH2*, *MSH6* (sequence and MLPA analysis), *EPCAM* (MLPA only)
- ☐ test for familial (likely) pathogenic variant

Hereditary nonpolyposis colorectal cancer (HNPCC) *(MLH1, MSH2, MSH6* gene*)* (MGPS) #

MSI- / Immunohistochemical analysis should be completed prior to molecular testing (please enclose copy of original report) (If possible please attach analysis report)
- ☐ complete variant screening in the *MLH1* gene incl. MLPA
- ☐ complete variant screening in the *MSH2* gene incl. MLPA
- ☐ complete variant screening in the *MSH6* gene incl. MLPA
- ☐ test for familial (likely) pathogenic variant (please enclose copy of original report)

Multiple endocrine neoplasia type1 (*MEN1*) #
- ☐ complete variant screening in the *MEN1 gene incl. MLPA*
- ☐ test for familial (likely) pathogenic variant (please enclose copy of original report)

Multiple endocrine neoplasia Typ2 (*MEN2*) #
- ☐ complete variant screening in the *RET* gene
- ☐ test for familial (likely) pathogenic variant (please enclose copy of original report)

Tuberous sclerosis (*TSC*) #
- ☐ complete variant screening in the *TSC1* and *TSC2* gene incl. MLPA
- ☐ test for familial (likely) pathogenic variant (please enclose copy of original report)

#: non accredited analysis

Type of specimen: **5-10 ml EDTA blood (children 3-5 ml) or DNA** (in case of karyotyping 3-5 ml NH_4 Heparin blood)
Please mark type of specimen with name and date of birth of the patient and send specimen at room temperature to:
***Laboratory for Molecular Genetic Diagnostics,* Institute of Human Genetics,**
Im Neuenheimer Feld 366, 69120 Heidelberg, Germany

Further diagnostic requests: See request forms
„Cytogenetik und Fluoreszenz in situ Hybridisierung (FISH) Diagnostik“ or „Leukämien und Lymphoproliferative Erkrankungen”

Declaration of consent (private patients)

Declaration of consent to joint billing (in accordance with the official medical fee schedule (GOÄ))

I consent that personal data of mine (i.e. address, date of birth, cost unit, diagnoses and services provided) may be transferred to, as well as processed and stored by *unimed Abrechnungsservice für Kliniken und Chefärzte GmbH* (accounting service for hospitals), Michael-Uwer-Straße 17-19, 66687 Waden, -in the following referred to as *unimed*- for the purpose of joint billing of private and elective medical laboratory services.

I herewith authorize *unimed* to collect outstanding claims in its own name, to commission registered legal service providers with the collection of overdue receivables and to obtain credit verification from credit enquiry agencies.

I acknowledge that the consent is given voluntarily and I am aware that granting or denying consent does not affect my medical treatment in any way. With this declaration I help saving significant additional expenses in the billing of services rendered. These savings help to improve the services offered by Heidelberg University Hospital.

By signing this declaration of consent, I expressly release the employees of Heidelberg University Hospital from their professional obligation to maintain secrecy towards *unimed*. *Unimed* employees are bound by a confidentiality obligation in respect to the processing of data and are subject to this even after termination of their employment. This is governed by §203 StGB. For further information on data protection please refer to: www.unimed.de

I can revoke my consent at any time and without giving reasons.
Please consider that the revocation only applies to the future. Processing which has been conducted prior to the revocation is not affected. After revocation, *unimed* is not entitled to process the data any further.

I acknowledge the receipt of information about the data processing and agree to my data being transferred to *unimed* GmbH.

……..... ……
Place, Date Signature of patient or his/her legal representative

……
Name in capital letter