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Your Results

Unique genetic insights to help get the right medicine, at the right dose, first time

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Pharmacogenetic profile - PGxProfile

Enclosed you will find your personal pharmacogenetic profile. This analysis was conducted to provide valuable insights into how your unique genetic predisposition may influence your response to certain medications.

Order information

Surname, first name:	**Date of birth:**	**Sample ID:**	**External ID:**
Doe, John	DD.MM.YYYY	IR15PGXDEMD100001	Insurance ID
Ordered by:	**Order date:**	**Order ID:**	**Report date:**
General practitioner	DD.MM.YYYY	IR56PGXDEMI100001	DD.MM.YYYY
Specimen details			
Sample type:	Saliva	**Sample arrival:**	DD.MM.YYYY

The following requirements for the pharmacogenetic test have been fulfilled:

1. Consent for the pharmacogenetic test
2. No bone marrow or stem cell, liver or kidney transplantation
3. No blood transfusion in the last four weeks

Digital phenotype profile

The digital phenotype profile can also be used in other PGXperts* applications. Please scan the QR code in the respective application.

*Further information can be found at www.pgxperts.com.

Introduction

This report contains the results of your pharmacogenetic test. As part of this pharmacogenetic test, we analysed which genetic characteristics (we refer to these as variants) are present in you and are potentially relevant to drug therapy safety.

Depending on the variants found, some active ingredients can be metabolised or excreted more quickly or more slowly and thus have a weaker or stronger effect. This could lead to side effects, hypersensitivity reactions or a lack of effect when taking these active ingredients. This can affect both current and potential future drug therapies. It is important to note that in addition to genetics, factors such as your weight, age, health and lifestyle can influence your response to medicines.

This report should therefore be presented to your doctor or other healthcare professionals so that they can customise your treatment to your personal circumstances. This may include, for example, the selection of the correct medication or a dose adjustment in order to optimise a current or planned therapy in the best possible way.

To ensure better readability, the term patient is used below to refer to the person being examined, regardless of gender or the reason for the pharmacogenetic examination.

WARNING!
If you're thinking about making any changes to your medication, we strongly recommend speaking with your healthcare professional first. Every person is different, and your treatment needs to be tailored to you. Changing your medication without medical advice could lead to problems like your condition getting worse or unwanted side effects

Contents of this report

1. Summary

In the summary you will find a list of all clinically relevant medicines known at the time of writing for which there are evidence-based recommendations for optimising drug therapy from national and international professional associations (e.g. CPIC, DPWG, SEFF) and regulatory authorities (e.g. EMA, FDA).

The summary is divided into medicines for which pharmacogenetic effects are available based on your PGx profile. These are also grouped according to severity.

The second part contains all medicines for which your PGx profile currently has no influence.

Medicines with known PGx effects

Severe pharmacogenetic effect

Please speak to your healthcare professional timely.

The use of this medicine is contraindicated and should be avoided. If you are taking any of the following Active ingredients, continue taking them as prescribed until you have spoken to your doctor.

abacavir	[Active ingredient]	[active ingredient] [active ingredient	[Active ingredient]

Moderate pharmacogenetic effect

It is advisable to have this checked by your healthcare professional.

These medicines may not work well for you or may cause side effects. If you are taking any of the following, continue to take them as prescribed until you have spoken to your healthcare professional.

allopurinol	azathioprine	flucloxacillin	mercaptopurine
tioguanine	[Active ingredient]	[Active ingredient]	[Active ingredient]

Mild pharmacogenetic effect

If you suspect side effects, please discuss these with your healthcare professional at your next appointment.

These medicines may not work well or may cause you mild side effects. If you are taking any of the following Active ingredients, continue taking them as prescribed until you have spoken to your doctor.

imatinib	rosuvastatin	[Active ingredient]	[Active ingredient]

Medicines without currently known PGx effects

acenocoumarol	amitriptyline	aripiprazole	atazanavir
atomoxetine	atorvastatin	brexpiprazole	brivaracetam
capecitabine	carbamazepine	carvedilol	celecoxib
cisplatin	citalopram	clomipramine	clopidogrel
codeine	dexlansoprazole	dextromethorphan	diazepam
doxepin	efavirenz	eliglustat	escitalopram
esomeprazole	flecainide	flucytosine	fluorouracil
fluoxetine	flurbiprofen	fluvastatin	fluvoxamine
fosphenytoin	gefitinib	glibenclamide	gliclazide
glimepiride	haloperidol	hydrocodone	ibuprofen
imipramine	irinotecan	lansoprazole	lornoxicam
lovastatin	mavacamten	meloxicam	metformin
methadone	metoprolol	mirtazapine	moclobemide
nevirapine	nortriptyline	omeprazole	ondansetron
oxaliplatin	oxycodone	pantoprazole	paroxetine
peginterferon alfa-2a	peginterferon alfa-2b	pegloticase	perphenazine
phenprocoumon	phenytoin	pimozide	piroxicam
pitavastatin	pitolisant	pravastatin	propafenone
quetiapine	rabeprazole	ribavirin	risperidone
rosuvastatin	sertraline	simvastatin	siponimod
tacrolimus	tamoxifen	tegafur	tenoxicam
tetrabenazine	thioridazine	tramadol	trimipramine
tropisetron	venlafaxine	voriconazole	vortioxetine
warfarin	zuclopenthixol		

2 Clinical implications

The medicines listed below may require a dose adjustment or alternative treatment. Please visit https://www.pgxperts.com/clinical-support for suggestions on alternative medicines. The recommendations refer to the standard dosage as described in the official prescribing guidelines (summary of product characteristics).

WARNING !
The content of this report is intended exclusively for healthcare professionals. Correct use of the service requires sound medical knowledge. The content provided does not replace medical advice. Changes to individual treatment without the consent of a doctor can lead to serious adverse drug reactions or treatment failure.

Serious pharmacogenetic effect
Absolute contraindication. A change in medication is indicated.

Active ingredient and gene	Clinical implications	Recommendations
Abacavir[1] *HCP5*	Increased risk of hypersensitivity.	Contraindication. An alternative medicinal product should be used.

Moderate pharmacogenetic effect
Consider dose adjustment, drug monitoring or a change of medication.

Active ingredient and gene	Clinical implications	Recommendations
Allopurinol *ABCG2*	Reduced response to therapy to be expected.	A dose increase of 40% of the recommended standard dose is indicated.
Azathioprine[1] *NUDT15-TPMT*	Significantly increased risk of severe myelotoxicity.	Malignant diseases: Dose adjustment is indicated. Non-malignant diseases: A change of medication should be considered. See footnote 4 for details.
Flucloxacillin *HCP5*	The risk of drug-induced liver damage is increased 80-fold.	All liver values should be checked at regular intervals. If the values are elevated, alternative medication is indicated.

Active ingredient and gene	Clinical implications	Recommendations
Mercaptopurine[1] *NUDT15-TPMT*	Increased or greatly increased risk of severe myelotoxicity.	Malignant diseases: Dose adjustment is indicated. Non-malignant diseases: A change of medication should be considered. Further information can be found in footnote 2.
Tioguanine[1] *NUDT15-TPMT*	Increased or greatly increased risk of severe myelotoxicity.	Malignant diseases: Dose adjustment is indicated. Non-malignant diseases: A change of medication should be considered. See footnote 3 for details.

Mild pharmacogenetic effect

In general, no Recommendations are required. Dose adjustment should be considered if symptoms occur.

Active ingredient and gene	Clinical implications	Recommendations
Imatinib *ABCG2*	A good molecular remission and therapy success are increased.	Start therapy with the lowest recommended starting dose.
Rosuvastatin *ABCG2*	An increased lipid-lowering effect can be expected.	Starting dose ≤ 20 mg or alternative statin or combination therapy indicated.

[1]At least one of the following organisations recommends or prescribes a genetic test before taking the active ingredient EMA, FDA, Swissmedic.

[2]In the case of non-malignant diseases, a switch to an alternative preparation that does not belong to the thiopurine group should be considered. In malignancies, a dose reduction to < 30-80% of the daily dose is indicated if the TPMT metaboliser is intermediate, provided that this is more than 75 mg/m²/day. For poor metabolisers of TPMT, in addition to reducing the initial dose to 10%, the frequency of administration should be reduced to three times per week. The dose should be adjusted according to the degree of myelosuppression and the disease-specific guidelines. A steady-state concentration is only reached 4-6 weeks after the respective dose adjustment. In case of myelosuppression, the reduction of the mercaptopurine dose has priority over other Active ingredients.

[3]In the case of non-malignant diseases, a switch to an alternative preparation should be considered. In the treatment of malignancies, a drastic dose reduction to 10 % of the standard dose is indicated. Instead of daily administration, the frequency of administration should be reduced to three times a week. The dose is adjusted according to the extent of myelosuppression and the disease-specific guidelines. A steady-state concentration is only reached 4-6 weeks after the respective dose adjustment. In cases of myelosuppression, the reduction of the tioguanine dose has priority over other Active ingredients.

[4]In non-malignant diseases, a switch to an alternative preparation should be considered. In the case of azathioprine therapy due to malignant disease, a drastic dose reduction to 10 % of the standard dose is indicated. Instead of daily administration, the frequency of administration should be reduced to three times a week. The dose should be adjusted according to the degree of myelosuppression and the disease-specific guidelines. A steady-state concentration is only reached 4-6 weeks after the respective dose adjustment.

3. Phenotype profile

The following table shows the expected phenotype (effect of the gene variants found) of the 26 genes or gene combinations analysed.

	Gene or gene combination	Diplotype[1]	Activity score	Expected phenotype[2]
1	*ABCG2*	rs2231142/rs2231142	Not defined	Poor function
2	*CYP2B6*	No variant detected	Not defined	Normal function
3	*CYP2C19*	No variant detected	Not defined	Normal metaboliser
4	*CYP2C9*	*1/*15	2	Normal metaboliser
5	*CYP2C9-VKORC1*	*1/*15, *1/rs9923231	Not defined	Undefined[3]
6	*CYP2C*	No variant detected	Not defined	Normal response
7	*CYP2D6*	No variant detected	2	Normal metaboliser
8	*CYP3A4*	No variant detected	Not defined	Normal metaboliser
9	*CYP3A5*	*3/*3	Not defined	Poor metaboliser (no CYP3A5 expression)
10	*CYP4F2*	No variant detected	Not defined	Normal metaboliser
11	*DPYD*	No variant detected	2	Normal metaboliser
12	*F5*	No variant detected	Not defined	Factor V Leiden negative
13	*G6PD*	No variant detected	Not defined	Normal function
14	*GSTP1*	No variant detected	Not defined	Normal metaboliser
15	*HCP5*	*1 /rs2395029	Not defined	HLA-B*57:01-positive
16	*HLA-A*31:01*	No variant detected	Not defined	HLA-A*31:01-negative
17	*HLA-B*15:02*	Variant undetermined	Not defined	Undefined[3]
18	*IFNL3*	No variant detected	Not defined	Favourable response genotype
19	*NUDT15*	No variant detected	Not defined	Normal function
20	*NUDT15-TPMT*	No variant detected, *3B/*3B	Not defined	Normal metaboliser / Poor metaboliser
21	*SLC22A1*	*5/*5	Not defined	Decreased function
22	*SLC22A2*	No variant detected	Not defined	Normal function
23	*SLCO1B1*	No variant detected	Not defined	Normal function
24	*TPMT*	*3B/*3B	Not defined	Poor metaboliser

25	*UGT1A1*	No variant detected	Not defined	Normal function
26	*VKORC1*	*1/rs9923231	Not defined	-1639 AG (Increased coumarin sensitivity)

[1]Diplotypes are characterised by the combination of two star alleles. This nomenclature, commonly used in pharmacogenetics, characterises a combination of variants. The star allele *1 generally characterises the absence of variants.

[2]The expected phenotype is a standardised term for the effect of an existing gene variant. The terms are based on information from the Clinical Pharmacogenetics Implementation Consortium (CPIC).

[3]There is insufficient evidence to pass on an expected phenotype (effect of the gene variant). Based on current knowledge, no predictions can be made regarding clinical implications and recommendations for affected medicines.

4. Laboratory results

Genotyping results

The genetic variants identified in the molecular biological analysis are listed below. A list of all analysed genetic variants can be found at the end of this chapter.

	Gene symbol	HGVS[1] Designation	Genotype	Zygosity
1	*ABCG2*	NC_000004.12:g.88131171G>T	T/T	Homozygous
2	*CYP3A5*	NC_000007.14:g.99672916T>C	C/C	Homozygous
3	*HCP5*	NC_000006.12:g.31464003T>G	T/G	Heterozygous
4	*HLA-B*15:02*	NC_000006.12:g.31313688T>C	AND	The result for the variant could not be determined
5	*SLC22A1*	NC_000006.12:g.160154805G>A	A/A	Homozygous
6	*TPMT*	NC_000006.12:g.18138997C>T	T/T	Homozygous

[1] Nomenclature of the Human Genome Variation Society

Number of gene copies

As a rule, two copies of the same gene are present. In individual cases, the loss of a single gene copy or a gene multiplication (more than two gene copies) can occur.

	Gene symbol	Target	Gene copies
1	*CYP2D6*	CYP2D6 exon 9	2

List of all analysed gene variants

Gene symbol	Variants
ABCG2	NC_000004.12:g.88131171G>T
CYP2B6	NC_000019.10:g.41009358A>G, NC_000019.10:g.41016810C>T, NC_000019.10:g.41004377A>G, NC_000019.10:g.41006936G>T, NC_000019.10:g.41012316T>C, NC_000019.10:g.41012339C>T, NC_000019.10:g.41006923C>T, NC_000019.10:g.40991224T>C, NC_000019.10:g.41006919C>G, NC_000019.10:g.41010006G>C, NC_000019.10:g.41006968T>G, NC_000019.10:g.41004015T>A
CYP2C9	NC_000010.11:g.94942290C>T, NC_000010.11:g.94981296A>C, NC_000010.11:g.94981297T>C, NC_000010.11:g.94981301C>G, NC_000010.11:g.94949283del, NC_000010.11:g.94936917T>C, NC_000010.11:g.94981224C>T, NC_000010.11:g.94941958T>C, NC_000010.11:g.94947782C>A
CYP2C19	NC_000010.11:g.94781859G>A, NC_000010.11:g.94780653G>A, NC_000010.11:g.94762706A>G, NC_000010.11:g.94852738C>T, NC_000010.11:g.94775453G>A, NC_000010.11:g.94781999T>A, NC_000010.11:g.94775416T>C, NC_000010.11:g.94775489G>A, NC_000010.11:g.94781858C>T, NC_000010.11:g.94852765C>T, NC_000010.11:g.94761900C>T, NC_000010.11:g.94775367A>G
CYP2D6	NC_000022.11:g.42127941G>A, NC_000022.11:g.42126611C>G, NC_000022.11:g.42127608C>T, NC_000022.11:g.42128242del, NC_000022.11:g.42128945C>T, NC_000022.11:g.42129084del, NC_000022.11:g.42127856T>G, NC_000022.11:g.42129033C>A, NC_000022.11:g.42128176_42128178del, NC_000022.11:g.42130692G>A, NC_000022.11:g.42129910C>G, NC_000022.11:g.42130668C>T, NC_000022.11:g.42129033C>T, NC_000022.11:g.42129770G>A, NC_000022.11:g.42126658_42126666dup, NC_000022.11:g.42128251_42128254del, NC_000022.11:g.42128817dup, NC_000022.11:g.42128218dup, NC_000022.11:g.42126749C>T, NC_000022.11:g.42128199_42128202TCAG[1], NC_000022.11:g.42128934AAAGGGGCG[3], NC_000022.11:g.42127803C>T, NC_000022.11:g.42127532_42127533dup, NC_000022.11:g.42127841C>G, NC_000022.11:g.42129075C>T, NC_000022.11:g.42127590G>A, NC_000022.11:g.42127852C>T
CYP3A4	NC_000007.14:g.99768693G>A
CYP3A5	NC_000007.14:g.99672916T>C, NC_000007.14:g.99665212C>T, NC_000007.14:g.99652771dup
DPYD	NC_000001.11:g.97450058C>T, NC_000001.11:g.97515787A>C, NC_000001.11:g.97082391T>A, NC_000001.11:g.97699474T>C, NC_000001.11:g.97579893G>C, NC_000001.11:g.97573863C>T
G6PD	NC_000023.11:g.154536002C>T, NC_000023.11:g.154535277T>C, NC_000023.11:g.154536168G>C, NC_000023.11:g.154534125C>A, NC_000023.11:g.154534125C>T, NC_000023.11:g.154533025A>G, NC_000023.11:g.154534440T>A, NC_000023.11:g.154534419G>A, NC_000023.11:g.154533044C>T, NC_000023.11:g.154532269C>A, NC_000023.11:g.154532269C>G, NC_000023.11:g.154535342C>T, NC_000023.11:g.154533596C>A/G, NC_000023.11:g.154532590G>C, NC_000023.11:g.154532695G>A, NC_000023.11:g.154533122C>T, NC_000023.11:g.154535190G>C
GSTP1	NC_000011.10:g.67585218A>G
HCP5	NC_000006.12:g.31464003T>G
*HLA-A*31:01*	NC_000006.12:g.29945521A>T
IFNL3	NC_000019.10:g.39252525T>G
NUDT15	NC_000013.11:g.48045719C>T, NC_000013.11:g.48037784GAGTCG[2]
SLC22A1	NC_000006.12:g.160154805G>A, NC_000006.12:g.160139851_160139853del
SLC22A2	NC_000006.12:g.160249250A>C
SLC47A1	NC_000017.11:g.19560030G>A
SLCO1B1	NC_000012.12:g.21178615T>C, NC_000012.12:g.21205999G>C, NC_000012.12:g.21176879C>A, NC_000012.12:g.21239042A>C,

	NC_000012.12:g.21176804A>G, NC_000012.12:g.21222355C>T, NC_000012.12:g.21200544C>G
TPMT	NC_000006.12:g.18143724C>G, NC_000006.12:g.18138997C>T, NC_000006.12:g.18130687T>C, NC_000006.12:g.18130781C>T
UGT1A1	NC_000002.12:g.233760973C>A, NC_000002.12:g.233760498G>A, NC_000002.12:g.233759924C>T
VKORC1	NC_000016.10:g.31096368C>T

5. Appendix

Laboratory information

Laboratory	Laboratory address	Website and e-mail
Eurofins Clinical Genetics	90 Pristley road Guildford GU2 7AU, UK	www.eurofins.co.uk/clinical-genetics GeneticEnquiriesUK@ctuk.eurofins.com

The patients' saliva samples were collected in GFX saliva collection tubes (Isohelix, GFX-01 IVD). DNA purification was performed using the Blood and Tissue DNA Kit (Omega, Mag-Bind CE IVD) on the KingFisher Flex System (Thermofisher). DNA quantification was performed using the Qubit - Broad Range dsDNA Quantification Kit and normalised to acceptable ranges. Genotyping was performed using the Infinium Global Screening Array with Enhanced PGx-48 v4.0 Kit (Illumina) and scanning with the iScan system (Illumina). Data analysis was performed with DRAGEN Array (Illumina) and reporting was performed with PGXperts software.

Scientific background

This pharmacogenetic report is generated based on the PGXperts database version that was current at the time of report creation (see system version in the footer). The PGXperts database is updated quarterly to reflect the evolving state of scientific knowledge; therefore, interpretations may change with future updates of the database. The pharmacogenetic effects presented here are only those supported by evidence-based knowledge at the time of this report's issuance.

The information contained in this report is based on scientific literature, including information and guidelines published by professional associations, e.g. the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Dutch Pharmacogenetics Working Group (DPWG), the Spanish Society of Pharmacogenetics and Pharmacogenomics (SEFF), the European Medicines Agency (EMA), the Food and Drug Administration (FDA), Health Canada Santé Canada (HCSC) and the Pharmaceuticals and Medical Devices Agency (PMDA) and SwissMedic.

Limitations

This report's applicability is explicitly limited to the patient's condition prior to any bone marrow, stem cell, liver, or kidney transplantation. Upon the patient undergoing such a transplant, the information and conclusions contained within this report become invalid due to the potential for altered genetic constitution.

The laboratory results do not recognise all variants in the genes tested, and the lack of detection of variants (designated *1 as common haplotype nomenclature in pharmacogenetics) does not exclude the presence of other, undetected variants. The tested variants can be looked up in the list of all analysed gene variants.

Other factors that may influence a patient's response to a drug that have not been considered in this report include environmental factors (e.g. air pollution), health factors (e.g. diet), social and family factors, age, gender, pregnancy, other genetic factors as well as various diseases and drug-drug interactions.

Disclaimer

The interpretations and clinical annotations provided by PGXperts are intended for use by healthcare professionals only and do not constitute medical advice by PGXperts. The administration of drugs, including those

listed in PGXperts reports, requires careful therapeutic monitoring, regardless of the phenotype or genotype-based interactions reported. The treating provider remains responsible for all diagnostic and treatment decisions for the patient.

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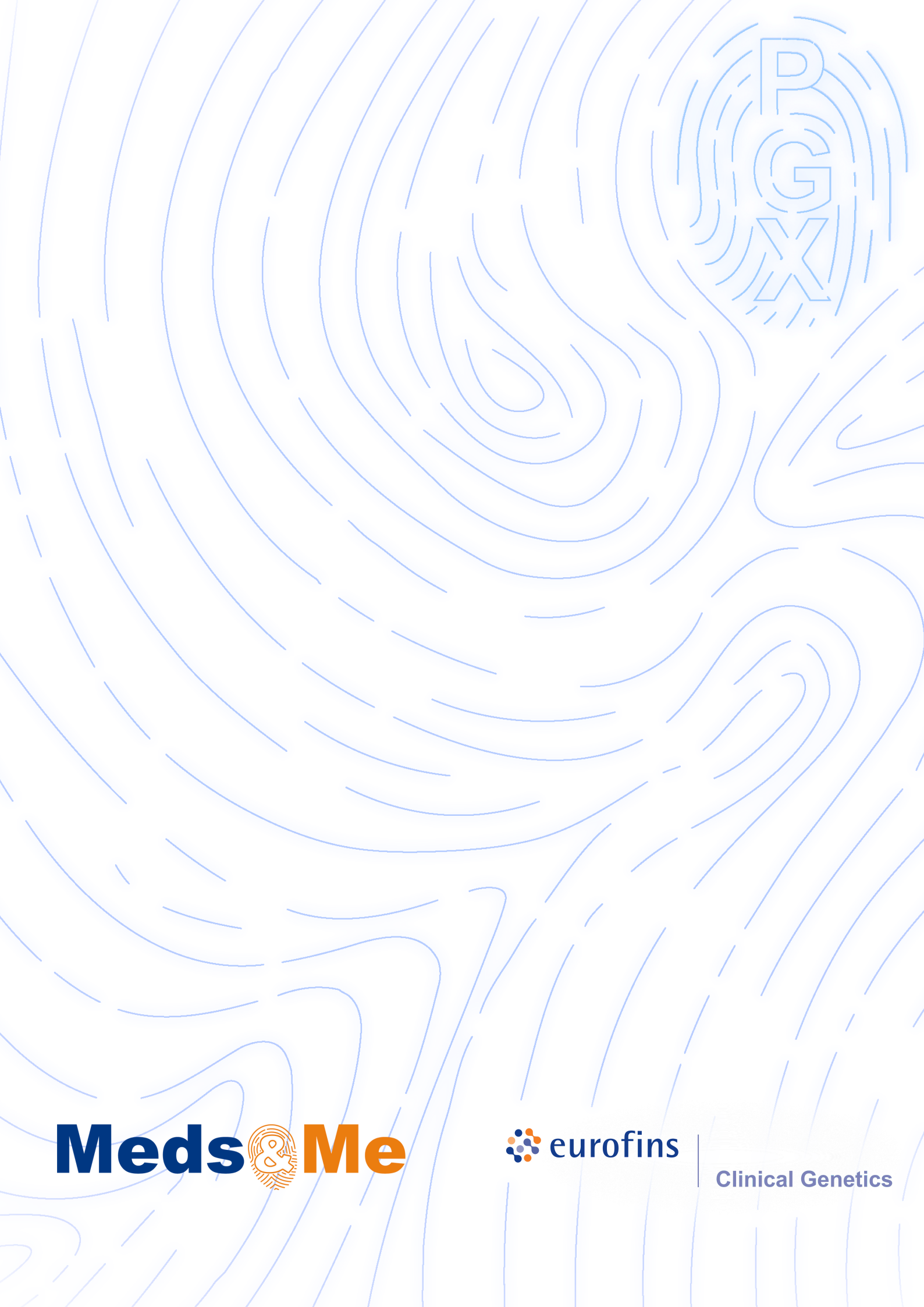
Authorised signatory

Job title: Date:

Name: Signature:



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