

# Coagulation - Pharmacogenomics

## PGX - Thrombo Strip Assay

Vitamin K antagonists (coumarins) are the most widely used oral anticoagulants for the prevention and treatment of venous thromboembolism, myocardial infarction and stroke. However, their narrow therapeutic range and wide inter-individual variability in dose response contribute to a considerable risk of adverse events during the first weeks to months of therapy. An inappropriate dosage can result in life-threatening complications, such as major bleeding in case of an overdose or incomplete prophylaxis from an insufficient dose. Careful monitoring of blood coagulation by measuring the prothrombin time, expressed as International Normalized Ratio (INR), is essential until a stable maintenance dose has been achieved.

Coumarin derivatives, such as warfarin (Coumadin<sup>®</sup>), phenprocoumon (Marcumar<sup>®</sup>) or acenocoumarol (Sintrom<sup>®</sup>), exert their therapeutic effect through inhibition of the vitamin K epoxide reductase. Polymorphisms in the target gene vitamin K epoxide reductase complex subunit 1 (VKORC1) are known to affect coumarin sensitivity. Moreover, variable rates of coumarin turnover due to polymorphisms in the drug metabolizing cytochrome P450 isozyme CYP2C9 also contribute to individual dose requirements.

The benefits of a pharmacogenetic approach to anticoagulation therapy are a more accurate *a priori* estimation of the coumarin maintenance dose, a decreased risk of inappropriate dosing during induction of therapy, and a reduction in time to achieve stabilization of therapy. A pharmacogenetic test for the prediction of coumarin dose requirements may therefore enable clinicians to provide a safer and more individualized anticoagulant treatment to their patients.



## PGX-Thrombo StripAssay:

ViennaLab offers a reliable and convenient reverse-hybridization assay for the prediction of coumarin dose requirement. The PGX-Thrombo StripAssay identifies a common polymorphism (-1639 G>A) in the VKORC1 promoter and two functionally impaired CYP2C9 variants (\*2 and \*3). Variations in these two genes, combined with certain physiological and lifestyle parameters (e.g. age, height, diet) account for more than 50% of variability in therapeutic coumarin dosage. The assay can assist clinicians to achieve a more individualized anticoagulant therapy, but does not substitute for monitoring blood coagulation (INR).

The PGX-Thrombo StripAssay provides ready-to-use reagents for 20 tests. The entire assay can be accomplished in less than 6 hours, and may be carried out manually or largely automated.

## Principle of the assay:

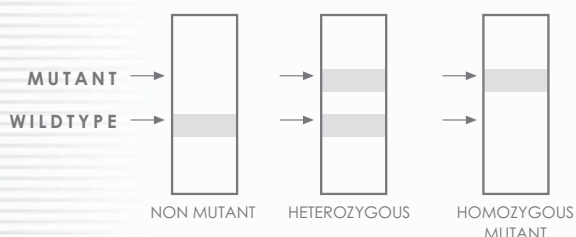
The PGX-Thrombo StripAssay is based on reverse-hybridization of biotinylated PCR products to a parallel array of allele-specific oligonucleotides immobilized on membrane teststrips. The StripAssay provides ready-to-use reagents for completion in four easy steps:

- Rapid and convenient isolation of genomic DNA from anticoagulated blood.
- Single multiplex PCR for the amplification of relevant VKORC1 and CYP2C9 gene sequences.
- Hybridization of biotinylated amplification products to oligonucleotide probes on the teststrip.
- Detection of specifically bound mutant and wild-type alleles by visible enzymatic color reaction.

## Interpretation of results:

For each polymorphic position, one of three possible staining patterns may be obtained:

1. wild-type probe positive: normal genotype
2. wild-type and mutant probe positive: heterozygous genotype
3. mutant probe positive: homozygous mutant genotype



Local contact:

## Polymorphisms covered by the ViennaLab PGX-Thrombo StripAssay:

VKORC1	Genotype	Coumarin sensitivity
-1639 G>A	GG	low
	GA	intermediate
	AA	high
CYP2C9	Genotype	Metabolic status
430 C>T (*2)	CC	extensive
	CT	intermediate
	TT	poor
1075 A>C (*3)	AA	extensive
	AC	intermediate
	CC	poor

## PGX-Thrombo StripAssay

Cat.no.: 4-730

**Further StripAssays are available or under development for:** Thalassemia ( $\alpha$ -Globin,  $\beta$ -Globin), Cardiovascular Disease (CVD), Familial Mediterranean Fever (FMF), Gaucher Disease, Haemochromatosis, Sugar Intolerance (lactose, fructose), Pharmacogenetics, Cancer.



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