

# CHROMOGENIX AB

K943111

## 510(k) Application COATEST® APC™ RESISTANCE

DEC 23 1996

### 510(k) SUMMARY

This summary of 510(k) safety and effectiveness is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

APC resistance is a newly detected abnormality in hemostasis, which appears to be prevalent in 20 % to 50 % of patients with deep venous thrombosis. This abnormality appears to be at least 10 times more common than inherited deficiencies of any of the other anticoagulant proteins.

APC resistance reflects an impairment of the expression of activated protein C (APC) activity in an individual's plasma and will result in a reduced ability to stop thrombin formation. The original device COATEST® APC™ RESISTANCE C / COATEST® APC™ RESISTANCE SC received 510(K) clearance for diagnosis of the APC resistance phenotype on August 8, 1995 (K945940). The new device COATEST® APC™ RESISTANCE V / COATEST® APC™ RESISTANCE V S contains a supplementary component, (factor) V-DEF Plasma. The present documentation intends to show the applicability of V-DEF Plasma in a modification of the original COATEST® APC™ Resistance kit and the sensitivity for the mutation in coagulation factor V is considerably increased. 90 to 95% of all cases with APC resistance are explained by a mutation in the factor V protein rendering the activated form of factor V less susceptible to degradation by APC. The documentation shows the applicability of V-DEF Plasma in a modification of the original COATEST® APC™ RESISTANCE kit with a considerably increased sensitivity for the mutation in factor V.

COATEST® APC™ RESISTANCE V or V S test is based on the use of activated protein C in an APTT clotting assay, as was the original test kit. Two studies support the substantially equivalency of COATEST® APC™ RESISTANCE V or V S (modified method) with COATEST® APC™ RESISTANCE (original method, K945940).

The first study shows a correlation (R= 0.74) between the two methods and their discrimination for FV:Q<sup>506</sup> on analysis of plasma from 218 acutely ill patients with suspected venous thrombosis or pulmonary emboli and from family members. The second study showed a similar correlation and discrimination for FV:Q<sup>506</sup>, noted above, between the two methods on analysis of plasma from 399 plasmapheresis donors. Thus, the data supports COATEST® APC™ RESISTANCE V or V S Substantial Equivalency to the predicated device COATEST® APC RESISTANCE C (K945940) and there is a high discrimination for FV:Q<sup>506</sup>.

The new method, COATEST® APC™ RESISTANCE V or V S, correlated well with regard to cases with thrombosis and with homo- or heterozygous factor V mutation. All showed pronounced APC resistance. The homozygous cases were properly discriminated from the heterozygous cases which were separated from the rest.

The safety and efficacy of COATEST® APC™ RESISTANCE V or V S is further supported by studies which show that this kit can be utilized on instruments with different clot detection principles and that appropriate results are obtained on analysis of plasmas from patients receiving oral anticoagulants, normal or low molecular weight (LMW) heparin or patients with the phospholipid antibody syndrome.

Thrombolyzer and MLA/Electra 900C, were utilized for samples of plasma from patients with myocardial infarction (97) and from healthy controls (132) in the former instrument; and on plasma from thrombotic patients or family members (50), in the latter instrument. The factor V gene nucleotide at

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position 1691 was determined in almost all individuals. A clear and complete discrimination is obtained for FV:Q<sup>506</sup> by both instruments and an improvement is obtained as compared to the original kit method. This is illustrated for the patient group. Evaluation of the 50 family members by the MLA/Electra 900C showed that for normal Factor V genotype an APC ratio of 2.4 - 3.4 was obtained, for the Heterozygous genotype 1.6 - 1.9 and for the Homozygous 1.2 to 1.3.

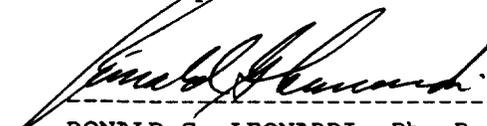
**COATEST<sup>®</sup> APC<sup>™</sup> RESISTANCE V or V S** was used for analysis of plasma from 147 patients on OAC therapy and 61 healthy controls by the ACL 300 and of plasma from 129 patients on OAC therapy and 62 healthy controls by the ST-4 instrument. The factor V gene nucleotide at position 1691 was determined in all.

Results show a clear discrimination obtained for the FV:Q<sup>506</sup> mutation on both ACL and ST-4. Similar ranges of APC ratios are obtained for healthy controls vs patients on OAC, for individuals with a normal factor V genotype, and with heterozygosity and homozygosity for FV:Q<sup>506</sup>, respectively. Results from the ACL and ST-4 instruments for plasmas from patients on unfractionated and low molecular weight (LMW) heparin at concentrations  $\leq 1$  IU/mL show that in contrast to the original method **COATEST<sup>®</sup> APC<sup>™</sup> RESISTANCE V or V S** provides normal APT times to at least 1 IU/mL of normal heparin. All samples from factor V genotyped patients receiving normal heparin were correctly classified as well as all of the genotyped LMW samples. The data also supports that a correct classification with regard to the factor V genotype is obtained for patients with the phospholipid antibody syndrome.

**COATEST<sup>®</sup> APC<sup>™</sup> RESISTANCE V or V S** provides a similar repeatability and reproducibility as Coatest APC Resistance. Similar results were obtained on the four instruments (Thrombolyzer, MLA/Electra 900, ST-4, ACL 300) included in the studies.

Calibration and Determination of the Cut-Off Value for the APC Ratio was performed with the **COATEST<sup>®</sup> APC<sup>™</sup> RESISTANCE V or V S** with three instruments in a population of normal factor V genotype males and females. The results illustrate that a significantly narrower range is obtained with **COATEST<sup>®</sup> APC<sup>™</sup> RESISTANCE V or V S** compared to the original Coatest APC Resistance kit. Further, based on the data presented and analyzed in the same manner as the original Kit, the results support the fact that the **COATEST<sup>®</sup> APC<sup>™</sup> RESISTANCE V or V S** has a greater than 99 % sensitivity for FV:Q<sup>506</sup>.

Reagent V-DEF Plasma and the stability of other reconstituted reagent was determined through the effect of storage at different temperatures on the APT time and the APC ratio on the analysis of plasmas containing factor V of different genotype origin. The above noted data support the assigned stabilities in the package insert of reconstituted V-DEF plasma. Further, a similar stability is obtained for 3 mL and 4 mL vials. Further, the data supports that whole blood and plasma can be stored for at least 7 hours at room temperature.

  
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