

Sigma ThromboMAX
510(k) Notification

Summary of Safety and Effectiveness

Sigma ThromboMAX™ with Calcium is a lyophilized preparation of thromboplastin derived from rabbit brain with buffers, stabilizers, and calcium ions. It is intended for use in the one-stage Prothrombin Time (PT) test and in PT based assays.

Thromboplastin is an extractable complex from many mammalian tissues which, in combination with calcium ions, accelerates the clotting of blood by activation of the extrinsic pathway of coagulation.^{1,2,3} This property lead to the development of a simple, rapid diagnostic assay now widely known as the Prothrombin Time (PT) test.^{4,5,6} The PT test is widely used as a pre-surgical screen for bleeding disorders and for monitoring anti-coagulant therapy.^{7,8} Dicumarol and related drugs reduce the activity of the vitamin K-dependent clotting factors II, VII, IX, X, Protein C, and Protein S^{9,10} and thereby prolong the PT. The PT assay is also used in the quantitative determination (Factor Assays) of Factors II, V, VII, and X.

The safety and effectiveness of Sigma ThromboMAX™ with Calcium (product numbers T9902, T6404, T5655, and T7655, herein referred to as "ThromboMAX" or abbreviated as "TP-MAX") has been demonstrated by showing it's substantial equivalence to Sigma Thromboplastin-XS (product numbers T9298 and T9423, herein referred to as "Thromboplastin-XS" or abbreviated as "TP-XS").

One hundred and one random patient samples were assayed on the Amelung CS-190 in both optical and mechanical modes with the described ThromboMAX reagent (y) and with the TP-XS reagent (x). Comparison of the results yielded correlation coefficients and regression equations of 0.979 and $y=0.870*x + 1.933$ for the optical method, and 0.980 and $y=0.86*x + 2.37$ for the mechanical method.

Fifteen random coumadin patient samples were likewise assayed, and comparison of the results yielded correlation coefficients and regression equations of 0.987 and $y=0.998*x - 1.97$ for the optical method, and 0.980 and $y=0.907*x - 0.47$ for the mechanical method.

Imprecision studies demonstrated the following within-run (S_{wr}) and total imprecision (S) coefficients of variation:

	CS-190 Optical		CS-190 Mechanical	
	$S_{wr} CV$	$S_t CV$	$S_{wr} CV$	$S_t CV$
<u>Control Plasma</u>				
Level I	0.46%	1.0%	0.9%	1.4%
Level II	0.45%	1.4%	1.72%	2.5%
Level III	1.43%	1.9%	2.00%	2.2%



Food and Drug Administration
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William R. Gilbert, Ph.D.
Manager, Scientific Affairs
Sigma Diagnostics®
545 South Ewing Avenue
St. Louis, Missouri 63103

OCT 10 1997

Re: K972796
Trade Name: Sigma ThromboMAX
Regulatory Class: II
Product Code: GJS
Dated: July 25, 1997
Received: July 28, 1997

Dear Dr. Gilbert:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

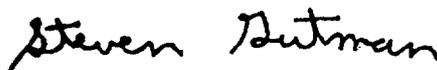
If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>"

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

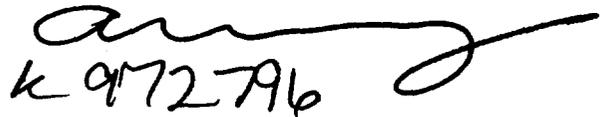
Enclosure

510(k) Number (if known): K972796

Device Name: Sigma Diagnostics ThromboMAX™ with Calcium

Indications For Use:

Sigma Diagnostics ThromboMAX™ with Calcium is a device used as a general screening procedure for the detection of possible clotting factor deficiencies in the extrinsic coagulation pathway which involves the reaction between coagulation factors III and VII, and to monitor patients receiving coumarin therapy (the administration of one of the coumarin anticoagulants in the treatment of venous thrombosis or pulmonary embolism).



K972796

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K972796

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use

Sigma ThromboMAX
510(k) Notification

References:

1. Quick, A.J., "On Various Properties of Thromboplastin (Aqueous Tissue Extracts), *Am. J. Physiology* 1936, 114: 282.
2. Nemerson, Y., "Characteristics and lipid requirements of coagulant proteins extracted from lung and brain; the specificity of the protein component of tissue factor", *J. Clin. Pathology* 1969, 48: 322.
3. Davie, E.W., Fujikawa, K., and Kisiel, W., "The Coagulation Cascade: Initiation, Maintenance, and Regulation", *Biochemistry* 1991, 30: 10363.
4. Quick, A.J., "The Prothrombin in Hemophilia and in Obstructive Jaundice", *J. Biol. Chemistry* 1935, 109: 73.
5. Quick, A.J., "The Nature of the Bleeding in Jaundice", *J. Am. Med. Assoc.* 1938, 110: 1658.
6. Quick, A.J., "Thromboplastin as a Reagent", *Thromb. Diath. Haemorrhage* 1970, 23: 585.
7. Errichetti, A.M., Holden, A., Ansell, J., "Management of Oral Anticoagulant Therapy: Experience with an Anticoagulation Clinic", *Arch. Inter. Medicine* 1984, 144: 1966.
8. Hirsh, J., Dalen, J.E., Deykin, D., Poller, L., "Oral Anticoagulants: Mechanisms of Action, Clinical Effectiveness, and Optimal Therapeutic Range", *Chest* 1992, 102 (suppl): 312S.
9. Miale, J.B., "Laboratory Medicine - Hematology, 4th edition", C.V. Mosby, St. Louis, 1972.
10. Furie, B., and Furie, B.C., "Molecular and Cellular Biology of Blood Coagulation", *N. Eng. J. Medicine* 1992, 326: 800.