K971039

510(k) Summary

JUN - 3 1997

1 Submitter's Name/Contact Person

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Date Prepared

7 March 1997

2 ***Device Names***

Trade Name:	Hemagen ® aCL Screen
Common Name:	anti Cardiolipin screening assay
Classification Name:	Immunological test system, multiple autoantibodies {21 CFR 866.5660}

3 ***Predicate Device(s)***

a. Hemagen ® Anti-Cardiolipin IgG and IgM {EIA method}
Reference 510 (k) Docket No. **K 932373**

b. Hemagen ® Anti-Cardiolipin IgA Calibrator Reagents {EIA method}
Reference 510 (k) Docket No. K **941840**

4 ***Description of Device***

The ELISA methodology is commonly used for serum antibody evaluations. In this assay, purified bovine cardiolipin has been attached to the inner surfaces of microplate test wells by the manufacturer. The user adds diluted patient samples to the wells. Anticardiolipin antibodies in patient serum bind specifically to the cardiolipin antigen attached to the plate, and remain in place after a wash step.

A trivalent second antibody cocktail, consisting of peroxidase-conjugated goat anti-human IgG (Fc), IgM (μ), and IgA (α), is added to the wells. After an incubation/wash step, TMB (tetramethylbenzidine) substrate is added. In the wells containing bound cardiolipin-anticardiolipin complexes, the peroxidase enzyme catalyzes a color change in the TMB substrate. After the reaction is stopped with dilute sulfuric acid, the color is read in an ELISA plate reader. Optical densities (ODs) of patient samples are compared to the OD of a reference serum included in the kit.

5 ***Intended Use of Device***

The device is intended for the qualitative detection of IgG, IgM, and IgA autoantibodies to cardiolipin in human serum.

6. ***Performance Data***

I. <u>Trivalent HRP Conjugate Standardization</u>

IgG, IgM, and IgA standard preparations (Louisville APL Diagnostics, Inc.) were diluted in Serum Diluent and tested with the predicate devices to establish standard curves. Optimal second antibody concentrations were established by titration for each monovalent HRP conjugate. The three conjugates were then blended, verified against the standard calibration curves, and freeze-dried.

II. <u>Cutoff Serum Standardization</u>

117 serum specimens from both disease state and normal patient panels were screened concurrently with both the proposed and predicate devices. Receiver Operating Characteristic {ROC}techniques were used to derive an optimized cutoff OD to be utilized in the preparation of the Cutoff Serum. Based upon this analysis and comparison testing, the optimized cutoff OD has demonstrated a relative analytical sensitivity of $\geq 97.0\ \%$

III. *Comparison Testing*

The Hemagen ® antiCardiolipin Screen , the Hemagen ® Anti-Cardiolipin IgG/ IgM assays, and the Hemagen ® Anti-Cardiolipin IgA Calibrator Reagents were used to concurrently assay serum specimens from patients positive for aCl, and from normal blood donors. A total of 117 samples were evaluated.

Table 1: Positive Panel, N = 38

		Predicate Devices		
		POS	NEG	TOTAL
Proposed Device	POS	38	0	38
	NEG	0	0	0
	TOTAL	38	0	38

Relative analytical sensitivity = 100 % {38/38}, 0.95 $_{INTERVAL}$ 90.8% to 100%

Table 2: Normal Panels, N=79

		Predicate Devices		
		POS	NEG	TOTAL
Proposed Device	POS	1	6	7
	NEG	0	72	72
	TOTAL	1	78	79

The indeterminate samples were retested with the proposed device.
The relative analytical specificity 92.3 % {72/78}, 0.95 $_{INTERVAL}$ 84.2 % to 96.4 %

Table 3: Combined Panels, N = 117

		Predicate Devices		
		POS	NEG	TOTAL
Proposed Device	POS	39	6	45
	NEG	0	72	72
	TOTAL	39	78	117

Relative sensitivity = 100 % {39/39} , 0.95 $_{INTERVAL}$ 91.0 % to 100 %
Relative specificity 92.3 % {72/78} , 0.95 $_{INTERVAL}$ 84.2 % to 96.4 %

IV. A. Precision

To evaluate anti Cardiolipin Screen precision, inter-assay and intra-assay studies were conducted.

Inter-assay precision
Three serum samples with various levels of anticardiolipin (negative, low positive, and high positive), the Cutoff Serum, and the Positive Control were assayed five times each, twice a day, on five different days:

Sample	Mean OD	Std. Dev.	CV
Negative	0.059	0.007	12.3 %
Low Positive	0.197	0.023	11.7 %
High Positive	0.967	0.067	6.9 %
Cutoff Serum	0.115	0.015	13.0 %
Positive Control	0.697	0.074	10.7 %

Intra-assay precision
Three serum samples with various levels of anticardiolipin (negative, low positive, and high positive) were assayed 16 consecutive times in a single run:

Sample	Mean OD	Std. Dev.	CV
Negative	0.069	0.010	15.0 %
Low Positive	0.306	0.022	7.1 %
High Positive	1.112	0.072	6.5 %

Conclusions

The results of the comparative studies support the claim that the Hemagen ® anti Cardiolipin Screen is substantially equivalent to the comparative devices, and performs as an effective screening assay for the detection of autoantibodies to anticardiolipin IgA, IgG, and IgM in human serum.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN - 3 1997

Mr. Joseph M. Califano
Manager, Regulatory Affairs
Hemagen Diagnostics, Inc.
34-40 Bear Hill Road
Waltham, Massachusetts 02154

Re: K971039
Trade Name: Hemagen® aCL Screen
Regulatory Class: II
Product Code: MID
Dated: March 20, 1997
Received: March 21, 1997

Dear Mr. Califano:

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 Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP 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 Gutman

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

Device Name: **Hemagen ® anti Cardiolipin Screen**

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Indication(s) For Use

The anti Cardiolipin Screen is indicated for the screening of patient serum for the presence of IgG, IgM, and IgA autoantibodies to cardiolipin . Autoantibodies to aCl are typically observed in patients with systemic lupus erythematosus and other connective tissue diseases. This assay is intended to be utilized as an aid in the diagnosis of antiphospholipid syndrome.

(PLEASE DO NOT WRITE BELOW THIS LINE)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Peter E. Maples

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

Prescription Use ✓ OR Over-The-Counter-Use___
(Per 21 CFR 801.109)