K974901

SEP 29 1998

510(k) SUMMARY

Submitter's Name, Address, Telephone Number, Contact Person and Date Prepared

Submitter
Digene Corporation
9000 Virginia Manor Road
Beltsville, MD 20705

Phone: (301) 470-6500
Facsimile: (301) 470-2881

Contact Person
Mark Del Vecchio
Associate Director, Regulatory and Clinical Affairs
Digene Corporation
Phone: (301) 470-6287
Facsimile: (301) 470-2881

Date Prepared: September 10, 1998

Name of Device and Name/Address of Sponsor

Name of Device
Hybrid Capture® System CMV DNA Assay

Sponsor
Digene Corporation
9000 Virginia Manor Road
Beltsville, MD 20705
Tel: 301-470-6500
Fax: 301-680-0696

Common or Usual Name

Hybrid Capture® CMV DNA Assay

Classification Name

Cytomegalovirus DNA Reagents

Predicate Devices

CMV Cell Culture (in use prior to May 28, 1976)
INCSTAR Corporation's CMV-vue™ Kit (K921616)

Device Description

The Hybrid Capture® CMV DNA Assay is a qualitative *in vitro* diagnostic assay. It is a nucleic acid, signal enhanced, solution hybridization, antibody capture assay that uses chemiluminescent signaling to detect CMV DNA. The assay kit consists of 13 reagents and two accessories.

Whole blood specimens are treated with an agent that lyses red blood cells, and the specimen is centrifuged, resulting in a pellet of white blood cells. The white blood cell pellet is then used in the Hybrid Capture CMV DNA Assay.

Specimens potentially containing CMV DNA are denatured and then hybridized with a specific CMV RNA probe cocktail. This cocktail contains a probe mixture chosen to eliminate cross-reactivity with human or other herpesvirus sequences. The CMV probe supplied with the Hybrid Capture CMV DNA Assay is complementary to approximately 40,000 base pairs or 17% of the CMV genome (230,000 base pairs).

The RNA:DNA hybrids resulting from hybridization are captured on the surface of a tube coated with affinity-purified polyclonal caprine antibodies specific for RNA:DNA hybrids. The immobilized hybrids are then reacted with alkaline phosphatase-conjugated, murine monoclonal antibody to RNA:DNA hybrids, and are detected with a chemiluminescent substrate. Several alkaline phosphatase molecules are conjugated to each antibody. Multiple conjugated antibodies bind to each captured hybrid, resulting in signal enhancement. As the substrate is cleaved by the bound alkaline phosphatase, light is emitted and is measured in Relative Light Units (RLUs) on a standard commercial luminometer. The RLU value of a specimen is compared to a Positive Cutoff Value and to an Equivocal Cutoff Value to determine if the specimen is positive, equivocal, or negative for the presence of CMV DNA.

Using a test panel consisting of dilutions of a stock solution of plasmid CMV DNA complementary to the CMV RNA probe (approximately 39,000 base pairs), the analytical sensitivity of the Hybrid Capture® CMV DNA Assay at the Positive Cutoff was determined to be 0.98 pg/mL (0.81 - 1.28). The analytical sensitivity of the assay at the Equivocal Cutoff was determined to be 0.48 pg/mL (0.40 - 0.63). Testing with a battery of blood-borne microorganisms, viruses, and human genomic DNA, as well as a collection of viruses known to be related to CMV, has demonstrated that the CMV probes used in the Hybrid Capture CMV DNA Assay are specific for CMV. A reproducibility study has shown that the Hybrid Capture CMV DNA Assay is reproducible over a range of CMV DNA concentrations, with acceptable within day, between days, between sites,

and overall percent coefficients of variation and standard deviations, as well as agreement in diagnostic outcome.

Clinical testing in HIV/AIDS patients and patients who had undergone a solid-organ or bone marrow transplants has demonstrated that the Hybrid Capture® CMV DNA Assay performs comparably to shell vial culture and cell culture in detecting CMV. Testing in a population comprised of approximately equal numbers of CMV seropositive and seronegative individuals has demonstrated that the assay is specific.

Intended Use

The Digene Hybrid Capture® CMV DNA Assay is a qualitative, *in vitro* diagnostic assay intended for the detection of human cytomegalovirus (CMV) DNA in human peripheral white blood cells isolated from whole blood specimens collected in EDTA. It is indicated for use as an aid in diagnosing CMV infection in solid organ transplant, bone marrow transplant and HIV/AIDS patients. This assay has not been cleared by the FDA for blood/plasma donor screening.

Technological Characteristics and Substantial Equivalence

The HC CMV DNA Assay is substantially equivalent to cell culture methods that were in use prior to May 28, 1976 for the isolation of CMV. While cell culture detects the replication of the microorganism, the HC CMV DNA Assay is intended to detect a component of the microorganism directly. The HC CMV DNA Assay is similar to cell culture methods in that white blood cells are used as specimens and in that controls are employed to ensure that reagents are working properly. Although the HC CMV DNA Assay is different from cell culture methods in its operating principles and technological characteristics, the effect of these differences can be assessed by comparing the number of CMV positives detected by each to expected results based on a combination of the cell culture result, the shell vial culture result, and clinical information. Parallel testing of specimens from solid organ transplant, bone marrow transplant and HIV/AIDS patients, has demonstrated that the HC CMV DNA Assay performs as well or better than cell culture in detecting CMV.

The Hybrid Capture® CMV DNA Assay is substantially equivalent to INCSTAR Corporation's CMV-vue™ Kit. The two assays have the same intended use and indications for use, detect a component of the cytomegalovirus, use whole blood from which white blood cells are isolated and tested, and include indirect immunoenzymatic procedures in their testing protocols. Although the assays have some differences in technological characteristics, the performance of these assays has been shown to be equivalent through testing clinical specimens and comparing the results to the same standard methods for CMV detection.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 29 1998

Mark Del Vecchio
Associate Director, Regulatory and
Clinical Affairs
Digene Corporation
9000 Virginia Manor Road
Beltsville, Maryland 20705

Re: K974901
Trade Name: Hybrid Capture System CMV DNA Assay
Regulatory Class: II
Product Code: LJO
Dated: September 10, 1998
Received: September 11, 1998

Dear Mr. Del Vecchio:

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 legally marketed predicate 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 requirements, 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 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

INDICATIONS FOR USE STATEMENT

510(K) Number (if known): **K974901**

Device Name: Digene Hybrid Capture® System CMV DNA Assay

Indications for Use:

The Digene *Hybrid Capture®* CMV DNA Assay is a qualitative, *in vitro*, diagnostic assay intended for the detection of human cytomegalovirus (CMV) DNA in human peripheral white blood cells isolated from whole blood specimens collected in EDTA. It is indicated for use as an aid in diagnosing CMV infection in solid organ transplant, bone marrow transplant and HIV/AIDS patients. This assay has not been cleared by the FDA for blood/plasma donor screening.

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANTOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Wooby Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K974901

Prescription Use X OR Over-The-Counter Use _____
(Per 21 CFR 801.109)