K990023

OCT 25 1999

510(k) SUMMARY

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

The assigned 510(k) number is: *N/A – This is a new 510(k)*

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

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Date Prepared: 1/4/99

Name of Device and Name/Address of Sponsor

Name of Device
Digene Hybrid Capture® II CT-ID Test

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

Common or Usual Name

HCII CT-ID Test

Classification Name

DNA Reagents, *Chlamydia*

Predicate Device(s)

The Gen-Probe® Pace® 2 System for Chlamydia Trachomatis cleared under K920378 on 4/29/92.

Device Description

The Digene HCII CT-ID Test is a nucleic acid, signal enhanced, hybridization, microplate assay using chemiluminescence for the qualitative detection of *C. trachomatis* (CT) DNA in cervical specimens collected using the Digene Cervical Sampler™ and in cervical specimens collected with a Dacron® swab and placed in Digene Specimen Transport Medium. The Digene HCII CT-ID Test is indicated for use as an aid in diagnosing infection with *C. trachomatis* in symptomatic or asymptomatic women. The HCII CT-ID Test may be used as a stand-alone test or may be used as a supplemental test to the Digene HCII CT/GC Test for identification of *C. trachomatis* in specimens that are positive by the HCII CT/GC Test.

Specimens potentially containing CT DNA are denatured and then hybridized with a specific RNA probe cocktail. This cocktail contains a probe mixture chosen to minimize or eliminate cross-reactivity with DNA sequences from human cells, other bacterial species, Chlamydia species other than *trachomatis*, or sequences from other microorganisms common in urogenital specimens. The CT probe cocktail supplied with the Digene CT-ID Assay is complementary to approximately 39,300 base pairs or 4% of the *C. trachomatis* genome (1×10^6 base pairs)[1] and 100% of the cryptic plasmid.

Steps and Reagents to Stabilize the Specimen:

Specimens are collected using the Digene Cervical Sampler or a Dacron Swab and placed in Digene Specimen Transport Medium (STM). The specimens may be held for up to two weeks at room temperature and shipped without refrigeration to the testing laboratory in an insolated container using an overnight or 2-day delivery vendor. At the testing laboratory specimens should be stored at 2-8°C if the assay is to be performed within one week. If the assay will be performed later than one week, the specimens should be stored at -20°C. A preservative has been added to the STM to retard bacterial growth and retain the integrity of DNA in the specimen. The STM is not intended to preserve the viability of organisms or other cells in the specimen.

Steps to Process the Specimen, Release the DNA, and Denature the Released DNA.

Denaturation reagent is added to the specimens with the collection device remaining in the collection tube. This allows for denaturation of any DNA clinging to the collection device. The volume of denaturation reagent added to the specimen is equivalent to one-half the volume of the specimen. The denaturation reagent is dilute sodium hydroxide. Specimens are then incubated for 45 minutes at 65°C. This step releases the DNA from the organisms contained in the specimen and denatures that DNA so it becomes single-stranded. Following this step, the single-stranded DNA is ready to be hybridized to the RNA probe.

[1] Kingsbury DT. Estimate of the genome size of various microorganisms. J Bacteriol 1969 Jun:98(3):1400-1.

The RNA:DNA hybrids resulting from hybridization are immobilized (captured) on the surface of a microplate-well, which has been coated with antibodies specific for RNA:DNA hybrids. The antibodies on the well surface capture the RNA:DNA hybrids. The immobilized hybrids are then reacted with alkaline phosphatase-conjugated antibody and a chemiluminescent substrate. As the substrate is cleaved by the bound alkaline phosphatase, photons are emitted and measured as Relative Light Units (RLUs) using a standard, FDA-cleared luminometer such as the DML 2000™. Increased photon emission, resulting in an enhanced signal, is achieved by conjugating multiple alkaline phosphatase molecules to each antibody molecule. Multiple antibodies bind to each RNA:DNA hybrid, further enhancing the signal.

The HCII CT-ID Test provides an RLU measurement that is qualitatively interpreted. The Positive Cutoff Value is equal to the mean of three Positive Control values. Each specimen RLU measurement is converted to a ratio of the Positive Cutoff Value. This conversion calculation is performed automatically by the Digene DML™ 2000 Microplate Luminometer software. Alternatively, the conversion may be calculated manually. Specimens with RLU/Cutoff values of < 0.8 are considered negative for CT DNA. Specimens with RLU/Cutoff values >5.0 are considered positive for CT DNA. Specimens with RLU/Cutoff values between $0.8 \geq 5.0$ are considered to be equivocal and are repeat tested in duplicate. With the repeat tests, a RLU/Cutoff Value of 1.0 is applied. If two of the three replicates fall above 1.0, the presence of *C. trachomatis* DNA is indicated. If at least two of the three replicates fall below 1.0, the presence of *C. trachomatis* DNA is not indicated.

Intended Use

The Digene HCII CT-ID Test, is a nucleic acid, signal enhanced, hybridization, microplate assay for the qualitative detection of *C. trachomatis* DNA in cervical specimens collected using the Digene Cervical Sampler™, or collected using a Dacron® swab and placed in Digene Specimen Transport Medium. The Digene HCII CT-ID Test is indicated for use as an aid in diagnosing infection with *C. trachomatis* in symptomatic or asymptomatic females. The HCII CT-ID Test may be used as a stand-alone test or may be used as a supplemental test for identification of *C. trachomatis* in specimens found positive by the Digene HCII CT/GC Test.

Technological Characteristics and Substantial Equivalence

The Digene HCII CT-ID Test is substantially equivalent to the Gen-Probe Pace® 2 System for *C. trachomatis* in intended use and in technological characteristics. Both tests are nucleic acid hybridization assays intended for the detection of chlamydia trachomatis from endocervical specimens.

A multicenter study has demonstrated that the Digene HCII CT-ID Test performs as well or better than the gold standard, cell culture, in detecting infection with *C. trachomatis* in the intended population. The results from this multicenter study are summarized below:

HCII CT-ID Test versus CT Culture/DFA

Symptomatic Patients

Brush Specimens

		CT-ID:	POS	POS	POS	NEG	NEG						
		Culture:	POS	NEG	NEG	POS	NEG						
2x2 Table Reference		DFA:	NA	POS	NEG *	NA	NA	Prevalence (%)	Sensitivity (95% CI)	Specificity (95% CI)	Ct-ID+/Cul-/DFA- Tested Positive by PCR	NPV (95% CI)	PPV (95% CI)
	Site	N											
18	UAB	351	42	5	7	2	295†	13.96	95.92 (86.0-99.5)	97.68 (95.3-99.1)	5/7	99.33 (97.6-99.9)	87.04 (75.1-94.6)
19	JHU	192	11	5	6	0	170	8.33	100.00 (79.4-100)	96.59 (92.7-98.7)	6/6	100.00 (97.9-100)	72.73 (49.8-89.3)
20	SUNY	220	34	0	3	1	182	15.91	97.14 (85.1-99.3)	98.38 (95.3-99.7)	1/2	99.45 (97.0-100)	91.89 (78.1-98.3)
21	UCSF	177	6	3	0	0	168	5.08	100.00 (66.4-100)	100.00 (97.8-100)	NA	100.00 (97.8-100)	100.00 (66.4-100)
22	***All***	***940***	***93***	***13***	***16***	***3***	***815***	***11.60***	***97.25 (92.2-99.4)***	***98.07 (96.9-98.9)***	***12/15***	***99.63 (98.9-99.9)***	***86.89 (79.6-92.3)***

* In two cases, DFA was required but not done.

† One CT-ID negative, culture negative specimen was unnecessarily tested by DFA and gave a positive result. This result was included in the performance calculations as a HCII CT-ID false negative.

CT-ID+/Cul- = specimens positive by the HCII CT-ID Test and negative by culture and negative by DFA. The data represented in this table are unresolved. The PCR data is provided for informational purposes only to show that most CT-ID+/Cul- specimens were positive by another molecular method.

HCII CT-ID Test versus CT Culture/DFA
Asymptomatic Patients
Brush Specimens

		CT-ID:	POS	POS	POS	NEG	NEG						
		Culture:	POS	NEG	NEG	POS	NEG						
2x2 Table Reference	Site	DFA: N	NA	POS	NEG	NA	NA	Prevalence (%)	Senstivity (95% CI)	Specificity (95% CI)	Ct-ID+/Cul-/DFA- Tested Positive by PCR	NPV (95% CI)	PPV (95% CI)
23	UAB	101	8	0	2	0	91	7.92	100.00 (63.1-100)	97.85 (92.5-99.7)	0/2	100.00 (96.0-100)	80.00 (44.4-97.5)
24	JHU	12	1	0	1	0	10	8.33	100.00 (2.50-100)	90.91 (58.7-99.8)	1/1	100.00 (69.2-100)	50.00 (1.3-98.7)
25	SUNY	81	3	0	0	0	78	3.70	100.00 (29.2-100)	100.00 (95.4-100)	NA	100.00 (95.4-100)	100.00 (29.2-100)
26	UCSF	236	9	1	4	0	222	4.24	100.00 (69.2-100)	98.23 (95.5-99.5)	3#/4	100.00 (98.4-100)	71.43 (41.9-91.6)
27	SJH	1	0	0	0	0	1	0	N/A	100.00 (2.5-100)		100.00 (2.5-100)	N/A
28	***All***	***431***	***21***	***1***	***7***	***0***	***402***	***5.10***	***100.00 (84.6-100)***	***98.29 (96.5-99.3)***	***4#/7***	***100 (99.1-100)***	***75.86 (56.5-89.7)***

In one case, PCR was not done.
CT-ID+/Cul- = specimens positive by the HCII CT-ID Test and negative by culture and negative by DFA. The data represented in this table are unresolved. The PCR data is provided for informational purposes only to show that most CT-ID+/Cul- specimens were positive by another molecular method.

HCII CT-ID Test versus CT Culture/DFA
Symptomatic Patients
Dacron®Swab Only

		CT-ID:	POS	POS	POS	NEG	NEG						
		Culture:	POS	NEG	NEG	POS	NEG						
2x2 Table Reference	Site	DFA: N	NA	POS	NEG	NA	NA	Prevalence (%)	Sensitivity (95% CI)	Specificity (95% CI)	CT-ID+/Cul-/DFA- Tested Positive by PCR	NPV (95% CI)	PPV (95% CI)
35	UAB	7	2	0	0	1	4	42.86	66.67 (94.3-99.2)	100 (39.8-100)	N/A	80.00 (28.4-99.5)	100.00 (15.8-100)
36	JHU	94	10	1	3	1	79	12.77	91.67 (61.5-99.8)	96.34 (89.6-99.2)	2/3	98.75 (93.2-99.9)	78.57 (49.2-95.3)
37	SUNY	8	1	0	0	2	5	37.50	33.33 (0.84-90.6)	100.00 (47.8-100)	N/A	71.43 (29.0-96.3)	100.00 (2.5-100)
38	SJH	152	7	0	2	0	143	4.61	100.00 (59.0-100)	98.62 (95.1-99.8)	0*/1	100.00 (97.5-100)	77.78 (40.0-97.2)
39	***All***	***261***	***20***	***1***	***5***	***4***	***231***	***9.58***	***84.00 (63.9-95.5)***	***97.88 (95.1-99.3)***	***2*/4***	***98.30 (95.7-99.5)***	***80.77 (60.7-93.5)***

* In one case DFA was required but not done.
\# In one case, PCR was not done.
CT/GC+/Cul- = specimens positive by Hybrid Capture II CT/GC Test and negative by culture and negative by DFA. The data represented in this table are unresolved. The PCR data is provided for informational purposes only to show that most CT/GC+/Cul- specimens were positive by another molecular method.

HCII CT-ID Test versus CT Culture/DFA
Asymptomatic Patients
Dacron®Swab Only

		CT-ID:	POS	POS	POS	NEG	NEG						
		Culture:	POS	NEG	NEG	POS	NEG						
2x2 Table Reference		DFA:	NA	POS	NEG	NA	NA	Prevalence (%)	Sensitivity (95% CI)	Specificity (95% CI)	CT-ID+/Cul-/DFA- Tested Positive by PCR	NPV (95% CI)	PPV (95% CI)
	Site	N											
40	UAB	1	1	0	0	0	0	100	100 (2.5-100)	NA	N/A	NA	100.00 (2.5-100)
41	JHU	10	0	0	0	0	10	0.0	NA	100 (69.2-100)	N/A	100.00 (69.2-100)	NA
42	SUNY	2	0	0	1	0	1	0.0	NA	50.00 (1.3-98.7)	N/A	100.00 (2.5-100)	0.00 (0-97.5)
43	UCSF	1	0	0	0	0	1	0.0	NA	100 (2.5-100)	N/A	100.00 (2.5-100)	NA
44	SJH	176	2	0	0	0	174	1.14	100.00 (15.8-100)	100.00 (97.9-100)	N/A	100.00 (97.9-100)	100.00 (15.8-100)
45	***All***	***190***	***3***	***0***	***1***	***0***	***186***	***1.58***	***100.00 (29.2-100)***	***99.47 (97.1-100)***	**N/A**	**100.00 (98.0-100)**	**75.00 (19.4-99.4)**

CT/GC+/Cul- = specimens positive by Hybrid Capture II CT/GC Test and negative by culture and negative by DFA. The data represented in this table are unresolved. The PCR data is provided for informational purposes only to show that most CT/GC+/Cul- specimens were positive by another molecular method.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT 25 1999

Mr. Mark A. Del Vecchio
Associate Director, Regulatory and Clinical Affairs
Digene Corpration
9000 Virginia Manor Road
Rockville, Maryland 20705

Re: K990023
Trade Name: Digene HCII CT-ID Test
Regulatory Class: I
Product Code: LSK
Dated: August 16, 1999
Received: August 17, 1999

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

510(k) Number (if known): K990023

Device Name: Digene HC II CT-ID

Indications For Use:

The Digene HCII CT-ID Test is an *in-vitro* nucleic acid hybridization assay with signal amplification using microplate chemiluminescence for the qualitative detection of *C. trachomatis* DNA in cervical specimens collected using the Digene Cervical Sampler™ (Cervical Brush and Specimen Transport Medium) and in cervical specimens collected using the Digene Swab Specimen Collection Kit (Dacron® swab and Specimen Transport Medium). The Digene HCII CT-ID Test is indicated for use with symptomatic or asymptomatic women as evidence of infection with *C. trachomatis.*

The HCII CT-ID Test may be used alone or as a supplemental test to the Digene HCII CT/GC Test to detect *C. trachomatis* DNA in specimens that are positive by the HCII CT/GC Test.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Wordy Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K990023

Prescription Use X
(Per 21 CFR 801.109)

OR

Over-The-Counter Use ___

(Optional Format 1-2-96)