FEB 29 2000

510(k) Summary

Hybrid Capture® II CT/GC DNA Test

K981567

INTENDED USE:

The Digene HCII CT/GC Test is an in vitro nucleic acid hybridization assay with signal amplification using microplate chemiluminescence for the combined qualitative detection of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (GC) DNA in cervical specimens collected with the Digene Cervical Sampler™ (Brush) and the Digene Swab Specimen Collection Kit (Swab). Follow-up testing using the Digene HCII CT-ID and HCII GC-ID Tests is required to identify the organism(s) present in HCII CT/GC DNA Test positive specimens. The HCII CT/GC DNA Test is indicated for use as an initial test to identify symptomatic or asymptomatic women with Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (GC) infection.

For *In Vitro* Diagnostic Use.

DESCRIPTION OF THE DEVICE:

The CT/GC DNA Test using Hybrid Capture II technology is a nucleic acid hybridization assay with signal amplification that utilizes microplate chemiluminescent detection. Specimens containing the target DNA hybridize with a specific CT/GC RNA probe cocktail. The resultant RNA:DNA hybrids are captured onto the surface of a microplate well coated with antibodies specific for RNA:DNA hybrids. Immobilized hybrids are then reacted with alkaline phosphatase conjugated antibodies specific for RNA:DNA hybrids, and detected with a chemiluminescent substrate. Several alkaline phosphatase molecules are conjugated to each antibody. Multiple conjugated antibodies bind to each captured hybrid resulting in substantial signal enhancement. As the substrate is cleaved by the bound alkaline phosphatase, light is emitted which is measured as relative light units (RLUs) on a luminometer. The intensity of the light emitted denotes the presence or absence of target DNA in the specimen.

An RLU measurement equal to or greater than a specified ratio to the positive Cutoff (CO) Value indicates the presence of Chlamydia and/or Neiserria DNA in the specimen. An RLU measurement less than a specified ratio to the positive Cutoff Value indicates the absence of Chlamydia and Neiserria DNA or Chlamydia and Neiserria DNA levels below the detection limit of the assay.

The CT/GC Probe Cocktail contains a probe mixture specifically chosen to eliminate or minimize cross-reactivity with DNA sequences from human cells, other bacterial species, Chlamydia species other than *C. trachomatis* or Neisseria species other than *N. gonorrhoeae*. The CT/GC Probe Cocktail supplied with the HCII CT/GC DNA Test is complementary to approximately 39,300 bp (4%) of the *Chlamydia trachomatis* genomic DNA (1×10^6 bp)[23] and 7,500 bp or 100% of the cryptic plasmid; and 9,700 bp (0.5%) of the *Neisseria gonorrhoeae* genomic DNA (1.9×10^6 bp)[24] and 4,200 bp or 100% of the cryptic plasmid. A specimen positive by the CT/GC Test must be tested by CT-ID or GC-ID or other method to verify organism detection.

SIMILARITIES AND DIFFERENCES TO PREDICATE DEVICE:

The Gen-Probe® Pace® 2 System for *Neisseria Gonorrhoeae* and *Chlamydia trachomatis* is the predicate device to which Digene claims the HCII CT/GC DNA Test is substantially equivalent. The Gen-Probe Pace 2 test is a legally marketed device made available for commercial distribution in the United States as of April 26, 1994 after FDA cleared 510(k) premarket notification K940979. Both the Pace 2 test and the Digene Hybrid Capture® II CT/GC DNA Test share the same intended use. Analytical and clinical data have been submitted to demonstrate that the Digene device is as safe and effective as the Gen-Probe® device.

NON-CLINICAL PERFORMANCE:

Precision

A precision study was performed at three sites to determine the within run and total precision of Digene's HCII CT/GC DNA Test using a panel of positive and negative masked, simulated clinical specimens. In addition, the intra- and inter-instrument precision observed with the two luminometers recommended for use with the HCII CT/GC DNA Test (Models DML2000 and MLX) was assessed using the same specimen panel.

Table 1 shows the performance of the Digene HCII CT/GC DNA Test for all sites combined. The qualitative results were 100% (54/54) (93.4%-100% 95%CI) in agreement with expected results at the three sites.

Table 1

Within Instrument, Between Instrument, Within Run, Total Precision Estimates For RLU/CO By Test and Target

			Within Instrument		***Between Instrument***		***Within Run***		***Total***	
Panel Member	*N*	*Mean*	*Standard Deviation (SD)*	*(%CV)*	*(SD)*	*(%CV)*	*(SD)*	*(%CV)*	*(SD)*	*(%CV)*
1	54	0.2152	0.0215	9.9767	0.0000	0.0000	0.1193	55.4447	0.1209	56.1831
2	54	0.2238	0.0432	19.3001	0.0000	0.0000	0.1102	49.2576	0.1219	54.4496
3	54	2.4554	0.1378	5.6129	0.0285	1.1620	0.2407	9.8019	0.2447	9.9648
4	54	3.5688	0.2099	5.8813	0.0753	2.1112	0.5905	16.5450	0.5869	16.4461
5	54	11.4036	0.5745	5.0375	0.3810	3.3409	1.3367	11.7217	1.3287	11.6516
6	54	15.9080	0.7444	4.6794	0.6632	4.1693	3.1325	19.6916	3.0769	19.3416

Analytical Sensitivity

The analytical sensitivity (limits of detection) of the *HCII CT/GC DNA Test* was determined by directly testing dilutions of a non-clinical panel consisting of 114 separate isolates of *Neisseria gonorrhoeae,* 15 serovars of *Chlamydia trachomatis*, 2 isolates of *Chlamydia psittaci* and 2 isolates of *Chlamydia pneumoniae.* The 114 isolates represented 13 auxotypes, 5 serovars, 10 antibiotic resistant strains, 2 plasmidless strains, and 2 uncharacterized isolates found discordant in the multicenter trial. Four point dilution series of the each of the serovars and auxotypes were tested using the *HCII CT/GC DNA Test* to establish the limits of detection for the test. For select *Chlamydia trachomatis* serovars testing was performed in triplicate under the original study design, which called for regression analysis to determine the limit of detection. Any additional testing was not performed in triplicate since regression analysis was not to be used for establishing the limit of detection.

The limit of detection for each Chlamydia serovar and *Neisseria gonorrhoeae* strain is summarized in Table 18. Based on these data, the LOD of the HCII CT/GC Test was determined to be 2500 *C. trachomatis* EB's/assay. This determination is limited by the ability of the HCII CT/GC Test to detect Chlamydia serovars E and J at 2500 EB's/assay. The lower limit of detection for all 15 CT serovars ranged from 50 - 2500 EB's/assay.

A paper by Lan, et al[29] suggested that the most common CT serovars in the United States for asymptomatic women less than 30 years old are E, I, and D (in decreasing order). For women aged 17-68 who were attending an inner city gynecological clinic, the most prevalent CT serovars encountered were F, E and G (in decreasing order). It is important to note that for the most commonly encountered CT serovars except serovars D and E, the Digene HCII CT/GC lower limit of detection was 50 EB's/assay; serovars D and E have higher limits of detection (500 EB's/assay for serovar D and 2500 EB's/assay for serovar E) as described earlier. The authors of this paper further suggest that certain serovars might be associated with symptomatic (i.e., serovar G) or asymptomatic (i.e., serovars D and I) infections. Again, for these serovars, the Digene HCII CT/GC Test demonstrated a lower limit of detection of 50 - 500 EB's/assay.

For the 114 Neisseria isolates, the lower LOD of the HCII CT/GC Test was determined to be 5000 organisms/assay. This determination is limited by the ability of the HCII CT/GC Test to detect two of five plasmidless isolates, one of 10 penicillin-resistant isolates, serovar IA-1 or IA-2, serovar IA-5, one spectinomycin resistant strain and one of five TRNG Dutch and TRNG American isolates at 5000 organisms/assay. The lower limit of detection for all 114 GC isolates ranged from 25 to 5000 organisms/assay.

Table 2

Summary of Organisms and Lower Limit of Detection in the HCII CT/GC DNA Test

Organism	Detectable Concentration	
	CFU/ml	CFUs/assay
N. gonorrhoeae Auxotype 1	1000	50
N. gonorrhoeae Auxotype 12	500	25
N. gonorrhoeae Auxotype 16	5000	250
N. gonorrhoeae Auxotype 22	50,000	2500
N. gonorrhoeae Auxotype 5	500	25
N. gonorrhoeae Auxotype 9	50,000	2500
N. gonorrhoeae Auxotype AHU	10,000	500
N. gonorrhoeae Auxotype Arg	10,000	500
N. gonorrhoeae Auxotype AU	1000 – 10,000	50 - 500
N. gonorrhoeae Auxotype PAU	1000 – 10,000	50 - 500
N. gonorrhoeae Auxotype Pro	10,000	500
N. gonorrhoeae Auxotype Proto	1000 – 10,000	50 - 500
N. gonorrhoeae Ciprofloxacin Intermediate (CipI)	1000 – 10,000	50 - 500
N. gonorrhoeae Ciprofloxacin Resistant (Cip R)	1000 – 10,000	50 - 500
N. gonorrhoeae CMRNG	1000 – 10,000	50 - 500
N. gonorrhoeae Other- 5423	10,000	500
N. gonorrhoeae Other- 5658	1000	50
N. gonorrhoeae PenR	10,000	500
N. gonorrhoeae Plasmidless strain Other	1000 – 100,000	50 - 5000
N. gonorrhoeae PPNG 3.05	10,000 – 100,000	500 - 5000
N. gonorrhoeae PPNG 3.2	10,000	500
N. gonorrhoeae PPNG 4.4	1000 – 100,000	50 - 5000
N. gonorrhoeae Serovar IA-1 or IA-2	10,000 – 100,000	500 - 5000
N. gonorrhoeae Serovar IA-5	10,000 – 100,000	500 - 5000
N. gonorrhoeae Serovar IB-1	1000 – 10,000	50 - 500
N. gonorrhoeae Serovar IB-4 or IB-15	10,000	500
N. gonorrhoeae Serovar IB-5	1000 – 10,000	50 - 500
N. gonorrhoeae Spectinomycin Resistant (SpeR)	100,000	5000
N. gonorrhoeae TetR	1000 – 10,000	50 - 500
N. gonorrhoeae TRNG American	10,000 – 100,000	500 - 5000
N. gonorrhoeae TRNG Dutch	10,000 – 100,000	500 - 5000
N. gonorrhoeae Type Strain	500	25

Table 2 (continued)

Summary of Organisms and Lower Limit of Detection in the HCII CT/GC Test

Organism	Detectable Concentration	
	EB's/ml	EB's/assay
Chlamydia trachomatis serovar A	10,000	500
Chlamydia trachomatis serovar B	10,000	500
Chlamydia trachomatis serovar Ba	5000	250
Chlamydia trachomatis serovar C	10,000	500
Chlamydia trachomatis serovar D	10,000	500
Chlamydia trachomatis serovar E	50,000	2500
Chlamydia trachomatis serovar F	1000	50
Chlamydia trachomatis serovar G	1000	50
Chlamydia trachomatis serovar H	10,000	500
Chlamydia trachomatis serovar I	1000	50
Chlamydia trachomatis serovar J	50,000	2500
Chlamydia trachomatis serovar K	20,000	1000
Chlamydia trachomatis serovar L1	2000	100
Chlamydia trachomatis serovar L2	2000	100
Chlamydia trachomatis serovar L3	5000	250

CLINICAL PERFORMANCE:

HCII CT/GC DNA Test performance characteristics were determined by comparing the assay results to results of *Chlamydia* and *Gonorrhea* culture and DFA testing. One thousand seven hundred eighty five (1785) specimens were collected and later tested from patients at 5 different sites including STD, Family Planning and OB/GYN clinics. DFA testing was performed on the sediment of the CT culture transport medium after centrifugation for specimens that were HCII CT/GC DNA Test-positive/culture-negative. The HCII CT/GC DNA Test results shown below in Table 3 were determined utilizing the HCII CT/GC DNA Test alone for each of the organisms specified. Specimens shown by culture/DFA to be infected with both CT and GC organism were analyzed separately and presented below as specimens with dual infection. The performance estimates shown do not take into consideration results obtained upon retesting with the HCII CT-ID DNA and HCII GC-ID DNA Tests.

As seen in Table 3, a total of thirty-seven specimens were observed as positive by initial CT/GC Testing and negative by both CT and GC culture. Among these 37 specimens, 13 were determined to be CT PCR positive, six were GC PCR positive, and one specimen was negative for both CT and GC PCR. PCR testing was not performed on the remaining specimens. Therefore overall, 51.4% (19/37) of these specimens were shown to contain either CT or GC DNA by PCR. In addition, all of these 19 specimens were retested according to the ID test verification algorithm and found to contain either CT and/or GC DNA with the HCII CT-ID DNA and HCII GC-ID DNA Tests.

Table 3

Summary of the Ability of the CT/GC Test Alone to Detect Individual Organisms

	n	***CT/GC Test***		
		Result		*Performance Estimate*
		POS	NEG	*Sensitivity (95% C.I.)*
Chlamydia trachomatis Culture/DFA Positive Alone	123	119	4	96.75% (91.9 – 99.1)
Nieserria gonorrhoeae Culture Positive Alone	84	78	6	92.86% (85.1 – 97.3)
Dual Infection (CT and GC Culture Positive)	31	31	0	100.00% (88.8 - 100)
Total Positive	**238**	**228**	**10**	**95.80% (92.4 - 98.0)**
				Specificity (95% C.I.)
Chlamydia trachomatis and *Nieserria gonorrhoeae* Culture Negative	1547	37	1510	97.61% (96.7 – 98.3)

Verification of CT/GC Positive Results with the CT-ID and GC-ID Tests

For the purposes of the summary presented in Table 4, the test results obtained from the testing of all specimens with the *HCII CT/GC DNA Test, HCII CT-ID DNA Test* and *HCII GC-ID DNA Test* were utilized. The results are stratified primarily by the results obtained initially with the CT/GC Test, and further stratified by the results obtained with the CT-ID and GC-ID Tests. Table 4 essentially expands on the data presented in Table 3, showing the distribution of the CT/GC, CT-ID, and GC-ID test results obtained for specimens in the clinical study found positive by CT culture alone (123), GC culture alone (84), the coinfected specimens (31), and specimens found negative by both CT and GC culture (1547). The data presented has been combined for all investigational sites, collection devices utilized and symptomology categories (symptomatic and asymptomatic patients) from the clinical trial.

Table 4

Summary of CT/GC Test Results
Symptomatic and Asymptomatic Patient Data Combined for All Investigational Sites

Culture Results	***CT+/GC+***	***CT+/GC-***	***CT-/GC+***	***CT-GC-***	***Total***
Digene CT/GC Positive					
CT-ID Positive (only)	2	115	0	15	132
GC-ID Positive (only)	1	0	75	9	85
CT-ID and GC-ID Positive	28	3	3	2	36
CT-ID and GC-ID Negative	0	1	0	11	12
Total	31	119	78	37	265
Digene CT/GC Negative					
CT-ID Positive (only)	0	1	0	8	9
GC-ID Positive (only)	0	0	0	10	10
CT-ID and GC-ID Positive	0	0	0	0	0
CT-ID and GC-ID Negative	0	3	6	1492	1501
Total	0	4	6	1510	1520
Total (both CT/GC pos and neg)	***31***	***123***	***84***	***1547***	***1785***

Performance Estimates – Sensitivity and Specificity of the CT-ID and GC-ID Verification System

A summary of the performance of the *HCII CT/GC DNA Test* when used in combination with the *HCII CT-ID DNA Test* and *HCII GC-ID DNA Test* is presented below. For these analyses, all specimens that tested positive by the *HCII CT/GC DNA Test* were further tested using the HCII CT-ID DNA and GC-ID DNA Tests and the results interpreted according to the retest algorithm defined in the section of this package insert entitled *Interpretation of Specimen Results*. This retesting algorithm is referred to as the "ID Verification System". By this definition, specimens that were CT/GC Test positive and negative by both the CT and GC ID tests were interpreted as negative. The sensitivity estimates for the CT and GC ID Verification systems can be found in Table 5 and the specificity estimates for both systems can be found in Table 6. Coinfected specimens were analyzed separately utilizing both systems so that performance when testing these types of specimens is clearly delineated. Overall, the sensitivity versus culture is only slightly lower when testing GC infected specimens when compared to testing CT infected specimens (93% versus 96%, respectively). These sensitivity estimates were determined relative to CT and GC Culture, which may have a sensitivity of 60-85%.

Of the 31 coinfected specimens identified by culture, the HCII CT/GC DNA test was positive for all 31. Twenty-eight of these were identified by *both* the CT-ID and GC-ID Test upon retesting to contain CT and GC DNA. For two of the three remaining coinfected specimens, only CT DNA was detected when retested with the ID assays (the GC-ID DNA Test was negative). In the last specimen, only GC DNA was detected (the CT-ID Test was negative for this specimen). See the "Coinfected Specimens" section below for further details.

The overall specificity for the CT and GC ID verification systems is also comparable, exceeding 98% for both systems as shown in Table 6. Table 6 also contains CT and GC PCR testing information for specimens that were found positive by the respective ID Verification system and negative by the corresponding culture method. PCR information is shown for informational purposes only; PCR test results were not used to resolve the test results obtained with the CT/GC Test system. Specific to the results for the CT-ID Verification system, 15/20, or 75%, of the apparent false positive results were determined by PCR to contain CT DNA, the remaining of which were not tested by CT PCR. Similarly for the GC-ID verification system, 50% (7/14) of the apparent false positive GC results were determined by PCR to contain GC DNA. Of the 1754 specimens from the clinical trial that were determined not to be coinfected, less than 0.5% (8/1754) were identified by the CT and GC ID Tests to contain both CT and GC DNA. Five of these eight specimens were tested by PCR and 4 were found to contain CT DNA and one was found to contain GC DNA. (see "Coinfected Specimens" section below for further details).

Tables 7 and 8 represent the performance of the CT and GC ID verifications systems stratified by testing site. Table 7 shows the sensitivity estimates versus CT and GC culture and Table 8 the specificity estimates versus CT and GC culture. In addition to individual testing site performance, each of these tables contains performance estimates for the sites grouped into two broad categories that reflect the characteristics of the patients populations tested. These broad categories are referred to as "High Positivity Rate" sites and "Low Positivity Rate" sites. The population enrolled at the High Positivity Rate sites was compromised primarily of patients attending STD clinics and included sites 1, 2, and 3. This accounts for the higher proportion of symptomatic patients observed at these three sites as compared to asymptomatic patients. Conversely, Sites 4 and 5, defined collectively as Low Positivity Rate sites, had a higher proportion of asymptomatic patients, since the patients in those populations were either from OB/GYN clinics or were attending clinics at the time of enrollment in the clinical study for reasons regarded as OB/GYN-related or routine in nature.

Table 5

CT/GC Test Performance Characteristics versus CT and GC Culture utilizing the CT-ID and GC-ID Test Repeat Testing Verification Algorithm

Sensitivity Estimate

Symptomatic and Asymptomatic Patient Data Combined for All Investigational Sites

Test	***Population***	***n***[1]	***No. infected***[2]	***Sensitivity*** *(95% Conf. Interval)*
CT-ID Verification System	*All CT infected*	148	154	96.10% (91.7 - 98.6)
	CT infection alone	118	123	95.93% (90.8 – 98.7)
	Coinfected	30	31	96.77% (83.3 – 99.9)
GC-ID Verification System	*All GC infected*	107	115	93.04% (86.8 – 97.0)
	GC infection alone	78	84	92.86% (85.1 – 97.3)
	Coinfected	29	31	93.55% (78.6 – 99.2)

1 Positive result as determined utilizing the CT/GC Test Repeat Testing ID Test Verification Algorithm as defined in the *Interpretation of Result* section of this product insert

2 As determined by CT culture, DFA, and/or GC culture

Table 6

CT/GC Test Performance Characteristics utilizing the CT-ID and GC-ID Test Repeat Testing Verification Algorithm

Specificity Estimate

Symptomatic and Asymptomatic Patient Data Combined for All Investigational Sites

		Negative Results			PCR Test Results[3]	
Test	**Population**	**CT/GC[1]**	**Culture[2]**	**Specificity** *(95% Conf. Interval)*	**CT Pos**	**GC Pos**
CT-ID Verification System	*No CT infection*	1611	1631	98.77% (98.1 – 99.3)	15/17	0/2
	No CT or GC infection	1530	1547	98.90% (98.3 – 99.4)	13/14	0/2
	GC infected	81	84	96.43% (89.9 – 99.3)	2/3	NA
GC-ID Verification System	*No GC infection*	1656	1670	99.16% (98.6 – 99.5)	2/3	7/10
	No CT or GC infection	1536	1547	99.29% (98.7 – 99.6)	1/2	6/8
	CT infected	120	123	97.56% (93.0 – 99.5)	1/1	1/2

1 As determined utilizing the CT/GC Test Repeat Testing ID Test Verification Algorithm as defined in the *Interpretation of Result* section of this product insert

2 As determined by CT culture, DFA, and/or GC culture

3 This information is provided for information only; specimen results were not resolved using PCR. PCR test results were not available for all apparent false positive specimens.

Table 7

CT/GC Test System Performance Characteristics

Sensitivity Estimates Stratified by Testing Site

	Site	***n***	***CT - ID Verification System***			***GC - ID Verification System***		
			All CT Infected	***CT Infection Alone***	*Coinfected*	*All GC Infected*	*GC Infection Alone*	*Coinfected*
	1	460	93.44 (57/61)	93.18 (41/44)	94.12 (16/17)	98.08 (51/52)	100 (35/35)	94.12 (16/17)
95% Conf. Int			84.1 - 98.2	81.3 - 98.6	71.3 - 99.9	89.7 - 100	90.0 - 100	71.3 - 99.9
	2	301	96.55 (28/29)	94.74 (18/19)	100 (10/10)	85.71 (30/35)	84.00 (21/25)	90.00 (9/10)
95% Conf. Int			82.2 - 99.9	74.0 - 99.9	69.2 - 100	69.7 - 95.2	63.9 - 95.5	55.5 - 99.8
	3	306	97.37 (37/38)	97.06 (33/34)	100 (4/4)	94.44 (17/18)	92.86 (13/14)	100 (4/4)
95% Conf. Int			86.2 - 99.9	84.7 - 99.9	39.8 - 100	72.7 - 99.9	66.1 - 99.8	39.8 - 100
	4	389	100 (17/17)	100 (17/17)	NA	88.89 (8/9)	88.89 (8/9)	NA
95% Conf. Int			80.5 - 100	80.5 - 100		51.8 - 99.7	51.8 - 99.7	
	5	329	100 (9/9)	100 (9/9)	NA	100 (1/1)	100 (1/1)	NA
95% Conf. Int			66.4 - 100	66.4 - 100		2.5 - 100	2.5 - 100	
High Positivity Rate Sites	1,2,3	1067	95.31 (122/128)	94.85 (92/97)	96.77 (30/31)	93.33 (98/105)	93.24 (69/74)	93.55 (29/31)
95% Conf. Int			90.1-98.3	88.4-98.3	83.3-99.9	86.8-97.3	84.9-97.8	78.6-99.2
Low Positivity Rate Sites	4,5	718	100 (26/26)	100 (26/26)	NA	90.00 (9/10)	90.00 (9/10)	NA
95% Conf. Int			86.8-100	86.8-100		55.5-99.8	55.5-99.8	
	All	1785	**96.10% (148/154)**	**95.93% (118/123)**	**96.77% (30/31)**	**93.04% (107/115)**	**92.86% (78/84)**	**93.55% (29/31)**
95% Conf. Int			**91.7 - 98.6**	**90.8 - 98.7**	**83.3 - 99.9**	**86.8 - 97.0**	**85.1 - 97.3**	**78.6 - 99.2**

Table 8

CT/GC Test System Performance Characteristics

Specificity Estimates Stratified by Testing Site

	Site	n	CT - ID Verification System			GC - ID Verification System		
			No CT infection	*No GC infection*	*GC infected*	*No GC infection*	*No CT infection*	*CT infected*
%	1	460	99.00% (395/399)	98.90% (360/364)	100% (35/35)	98.77% (403/408)	98.90% (360/364)	97.73% (43/44)
95% Conf. Int			97.5 - 99.7	97.2 - 99.7	90.0 – 100	97.2 - 99.6	97.2 - 99.7	88.0 - 99.9
%	2	301	97.06% (264/272)	97.57% (241/247)	92.00% (23/25)	98.87% (263/266)	98.79% (244/247)	100% (19/19)
95% Conf. Int			94.3 - 98.7	94.8 - 99.1	74.0 - 99.0	96.7 - 99.8	96.5 - 99.8	82.4 – 10
%	3	306	98.88% (265/268)	99.21% (252/254)	92.86% (13/14)	98.96% (285/288)	99.21% (252/254)	97.06% (33/34)
95% Conf. Int			96.8 - 99.8	97.2 - 99.9	66.1 – 99.8	97.0 - 99.8	97.2 - 99.9	84.7 - 99.9
%	4	389	98.92% (368/372)	98.90% (359/363)	100% (9/9)	99.47% (378/380)	99.45% (361/363)	100% (17/17)
95% Conf. Int			97.3 - 99.7	97.2 - 99.7	66.4 – 100	98.1 - 99.9	98.0 – 9.9	80.5 – 100
%	5	329	99.69% (319/320)	99.69% (318/319)	100% (1/1)	99.70% (327/328)	100% (319/319)	8.89% (8/9)
95% Conf. Int			98.3 – 100	98.3 – 100	2.5 – 100	98.3 – 100	98.9 – 100	51.8 – 99.7
High Positivity Rate Sites	1,2,3	1067	98.40 (924/939)	98.61 (853/865)	95.95 (71/74)	98.86 (951/962)	98.96 (856/865)	97.94 (95/97)
95% Conf. Int			97.4-99.1	97.6-99.3	88.6-99.2	98.0-99.4	98.0-99.5	92.8-99.8
Low Positivity Rate Sites	4,5	718	99.28 (687/692)	99.27 (677/682)	100 (10/10)	99.58 (705/708)	99.71 (680/682)	96.15 (25/26)
95% Conf. Int			98.3-99.8	98.3-99.8	69.2-100	98.8-99.9	98.9-100	80.4-99.9
	All	1785	***98.77% (1611/1631)***	***98.90% (1530/1547)***	***96.43% (81/84)***	***99.16% (1656/1670)***	***99.29% (1536/1547)***	***97.56% (120/123)***
95% Conf. Int			***98.1 - 99.3***	***98.3 - 99.4***	***89.9 - 99.3***	***98.6 - 99.5***	***98.7 - 99.6***	***93.0 - 99.5***

Coinfected Specimens

Of particular interest are the 31 specimens determined positive by CT culture/DFA and GC culture to be coinfected with these organisms. Although not evident from Tables 5 or 6, CT or GC DNA was detected in all 31 of these coinfected specimens with the CT/GC Test. Of the 31 CT/GC Test positive specimens, 28 (90%) were verified by both the CT-ID and GC-ID Tests to contain CT and GC DNA as previously indicated, leaving only 3 specimens (10%) that were not detected from patients with dual infections. The CT-ID Test detected two of these three coinfected specimens and the GC-ID Test detected one of the coinfected specimens.

Conversely, only eight specimens identified as positive by all three HCII Tests were not verified by culture or DFA to contain both organisms. This included only two specimens that were negative by both CT and GC culture, however, one of the specimens (specimen 1 in Table 9) was positive for CT DNA by PCR. If PCR test results are taken into consideration, this reduces the number of unconfirmed CT/GC Test system coinfected specimens to five.

Table 9
Specimens Positive by All Three HCII Tests and Unconfirmed as Coinfected with CT and GC DNA by CT Culture/DFA and GC Culture (n=8)

No.	*CT Culture /DFA*	*GC Culture*	*PCR Results*	
			CT	*GC*
1.	NEG	NEG	POS	NEG
2.	NEG	NEG	NEG	NEG
3.	NEG	POS	POS	ND
4.	NEG	POS	NEG	ND
5.	NEG	POS	POS	ND
6.	POS	NEG	POS	NEG
7.	POS	NEG	ND	POS
8.	POS	NEG	ND	ND

Prevalence

The positivity rates observed among the clinical study population for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* when viewed collectively using the *HCII CT/GC DNA Test* ranged from 1.7% to 22.7% (Table 10). The data in Table 10 represent the number of patients from which CT DNA and GC DNA, and both CT and GC DNA (coinfected) were detected and the percent verified as positive by retesting initial CT/GC Test positive specimens with the *HCII CT-ID DNA* and *GC-ID Tests*. The positivity rate data provided are stratified by testing site and presence or absence of symptoms observed in the patient from which specimens were collected. In general, the positivity rates for the individual detection of CT DNA (not including co-infected patients) were consistent amongst the testing sites in the asymptomatic patient population; however, the individual GC DNA positivity rates did vary more significantly in this population. Among the symptomatic patients, sites 1 through 3 demonstrated a higher rate of positivity for both CT and GC infection (>5%) as compared to sites 4 and 5. The variation observed in the positivity rates when determining the presence of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* are influenced by population characteristics such as age, sex, and risk factors.

Table 10

Positivity Rates using the CT/GC Test and the CT-ID and GC-ID Test Verification System

			ID Test System Results							
Population	***Test Site***	***n***	***CT-ID Positive only***		***GC-ID Positive Only***		***CT-ID and GC-ID Positive (Coinfected)***		***CT-ID and/or GC-ID Positive***	
			No. Pos	*% Pos*	*No. Pos*	*% Pos*	*No. Pos*	*% Pos*	*No. Pos*	*% Pos*
Symptomatic	1	358	36	10.1	29	8.1	11	3.1	76	21.2
	2	279	17	6.1	17	6.1	9	3.2	43	15.4
	3	223	30	13.5	12	5.4	4	1.8	46	20.6
	4	162	7	4.3	4	2.5	0	0.0	11	6.8
	5	152	7	4.6	0	0.0	0	0.0	7	4.6
	All	1174	97	8.3	62	5.3	24	2.0	183	15.6
Asymptomatic	1	102	5	4.9	6	5.9	4	3.9	15	14.7
	2	22	1	4.5	4	18.2	0	0.0	5	22.7
	3	83	3	3.6	1	1.2	0	0.0	4	4.8
	4	227	10	4.4	4	1.8	0	0.0	14	6.2
	5	177	2	1.1	1	0.6	0	0.0	3	1.7
	All	611	21	3.4	16	2.6	4	0.7	41	6.7
Total		1785	118	6.6	78	4.4	28	1.6	253	14.2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 29 2000

Mr. Mark A. Del Vecchio
Associate Director, Regulatory and Clinical Affairs
Digene Corporation
1201 Clopper Road
Gaithersburg, Maryland 20878

Re: K981567
Trade Name: Digene Hybrid Capture® II CT/GC DNA Test
Regulatory Class: II
Product Code: LSL, LSK
Dated: January 14, 2000
Received: January 18, 2000

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.

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" (21CFR 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 (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/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): K981567

Device Name: Digene Hybrid Capture® II CT/GC DNA Test

Indications for Use:

"The Digene HCII CT/GC Test is an in vitro nucleic acid hybridization assay with signal amplification using microplate chemiluminescence for the combined qualitative detection of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (GC) DNA in cervical specimens collected with the Digene Cervical Sampler™ (Brush) and the Digene Swab Specimen Collection Kit (Swab). Follow-up testing using the Digene HCII CT-ID and HCII GC-ID Tests is required to identify the organism(s) present in HCII CT/GC DNA Test positive specimens. The HCII CT/GC DNA Test is indicated for use as an initial test to identify symptomatic or asymptomatic women with Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (GC) infection.

For *In Vitro* Diagnostic Use."

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K981567

Prescription Use ✓ OR Over-The-Counter Use NO
(Per 21 CFR 801.109)