DEC 17 2004

12.0 510(k) Summary of Safety and Effectiveness

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

510(k) Number: ***K042676***

12.1. Name of Submitter, Contact Person and Date Summary Prepared:

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Date Prepared: 7/21/2004

12.2. Device Name

Trade/Proprietary Name:	Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay
Common/Usual Name:	Nichols Advantage® H-hCG Assay
Classification Name:	System, Test, Human Chorionic Gonadotropin (hCG)

12.3. Predicate Device

Substantial equivalence is claimed to the DPC's IMMULITE® hCG Immunoassay (K990222; Cleared 2/26/99).

12.4. Device Description

The Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin Assay (i.e., Nichols Advantage® H-hCG Assay) is a two-step, two-site immunochemiluminometric assay for use with the Nichols Advantage® Specialty System, for the measurement of H-hCG as an aid in the detection of pregnancy. This new Nichols Advantage® H-hCG Assay [as with the predicate of the Diagnostic Products Corporation (= DPC) termed: the DPC IMMULITE® hCG Immunoassay (K990222; cleared 2/26/99)] is a two-step, two-site immunochemiluminometric assay for use with the Nichols Advantage® Specialty System.

12.5. Intended Use

The Nichols Advantage Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay (or simply: **Nichols Advantage® H-hCG Assay**) is intended for use with the Nichols Advantage® Specialty System for the quantitative measurement of hyperglycosylated human chorionic gonadotropin (H-hCG), a placental hormone in human serum, or for the qualitative determination of H-hCG in urine as an aid in the detection of pregnancy. These diagnoses should be made with appropriate additional clinical evidence. Clinical considerations and professional judgment should

be applied to any test device result, particularly when preliminary positive results are obtained, as with this Nichols H-hCG chemiluminescent immunoassay.

The Nichols Advantage® H-hCG Assay is used in conjunction with two H-hCG calibrators which are used to calibrate the assay and are provided separately to the reagent cartridge. The control is used for the monitoring of the accuracy and precision of the Nichols Advantage H-hCG Assay and successful calibration is confirmed using three H-hCG controls also provided separately to the calibrators and reagent cartridge.

12.6. Comparison to predicate device

The Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay is substantially equivalent to other laboratory based pregnancy assay products in commercial distribution for similar use. Most notably, it is substantially equivalent to the DPC IMMULITE hCG Immunoassay. The following tables compare the Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay with the predicate device, the DPC IMMULITE hCG Immunoassay.

Comparison Summary with Predicate Device		
Similarities		
Feature	**Nichols Advantage H-hCG New Assay**	**DPC IMMULITE 2000 hCG Predicate Immunoassay**
Antibody Recognition	Specific antibodies that bind isoforms of hCG	Specific antibodies that bind isoforms of hCG
Sample Type	Assay utilizes human serum or urine as test samples	Assay utilizes human serum or urine as test samples
Analysis Technology	Utilizes chemiluminescent technology for quantitation with assay incubated to 37°C.	Utilizes chemiluminescent technology for quantitation with assay incubated to 37°C.
Sensitivity	Sensitivity & critical detection limit sufficient to utilizes human serum or urine for hCG isoforms in determination of pregnancy	Sensitivity & critical detection limit sufficient to utilizes human serum or urine for hCG isoforms in determination of pregnancy
Interferences - serum	High limits for interference from serum a) protein, b) bilirubin, c) triglycerides, and d) free serum hemoglobin	High limits for interference from serum a) protein, b) bilirubin, c) triglycerides, and d) free serum hemoglobin
Interferences - urine	High limits for interference from urine glucose via severe diabetes.	High limits for interference from urine glucose via severe diabetes.

Differences		
Feature	**Nichols Advantage H-hCG New Assay***	**DPC IMMULITE 2000 hCG Predicate Immunoassay**
Antibody Recognition	Monoclonal antibodies that recognize H-hCG*	Monoclonal antibodies that recognize hCG
Sample Volume	15 microliters	5 microliters
Reporting Unit	ng/ml* [for H-hCG, based on Mass units of ng per ml serum]	mIU/ml [for hCG, based on milli-International Units]

* The Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay reports values in ng/ml. The correlation for the reporting units of the predicate device compared to NID is expressed by Y(DPC's) = -5.36 + 28.32X(NID's) with correlation factor r= 0.935, P-Value < 0.001.(page 109)

12.7. Test Principle

Both Assays utilize Competition Assays and Immunometric Assays with chemiluminescence for detection and quantitation. A summary of a technological comparison of each method's test principles is presented in the following **Table of Technology Comparisons:**

Table of Technology Comparisons		
	New Device	**Predicate Device**
ITEM	**Nichols Advantage H-hCG Assay**	**DPC IMMULITE hCG Assay**
Test Principle	Immunochemiluminometric sandwich assay using biotinylated and acridinium ester-labeled mouse monoclonal anti-H-hCG antibodies coated on magnetic particles for capture and detection	Immunochemilumin assay using monoclonal antibody coated polystyrene bead for capture and subsequent detection.
Sample Dilution	Operator selectable, sample-specific on-board dilutions	None described in directional insert
Tracer	Acridinium ester-labeled mouse monoclonal anti-H-hCG antibody	Alkaline phosphatase conjugated to poly- clonal ovine (sic) anti-hCG antibody
Antigen Used in Standards	H-hCG derived from JEG-3 cell line calibrated vs. C5 [Columbia University & NIH, Bethesda, MD]	WHO 3rd IS 75/573
Separation System	Streptavidin-coated magnetic particles	Anti-hCG beta subunit-coated polystyrene bead
Incubation	Number of Incubations: Two Incubation Period 1: 30 minutes Incubation Temperature: 37°C Incubation Period 2: 10 minutes Incubation Temperature: 37°C	Number of Incubations: Two Incubation Period 1: 30 minutes Incubation Temperature: 37°C Incubation period:2: 5 min. Incubation temperature: 37°C.

12.8. Performance Characteristics:

12.8.1. Analytical performance –

12.8.1.a. Precision/Reproducibility:

The patient or patient pool samples were evaluated by an accelerated format of the NCCLS EP-5 protocol; two replicates of each specimen run on each of four assays per day over a 10 day period. This format yields 80 data points, which will be analyzed according to the NCCLS EP-5 algorithm statistic. The Nichols Advantage® H-hCG Assay average CV for the total precision shall be no more than 2% higher than the corresponding CV of the predicate IMMULITE 2000 hCG Assay. The Nichols H-hCG Assay average total inter-assay precision was 6.7% C.V; the Acceptable Criteria was considered a high of: 7.22% C.V.

12.8.1.b. Linearity/assay reportable range:

A linear correlation comparison study of critical values for pregnancy determination using this new **Nichols H-hCG Assay** (X) was carried out versus the cleared (K990222, 5/27/99) predicate DPC Immulite 2000 hCG Assay (Y) for n = 61 apparently pregnant and health female subjects [i.e., those reporting 0 to 2 weeks of gestation]. Analysis of the resulting data gave a linear regression correlation equation that was acceptable for values ranging from 0.2 to 27 ng/mL for H-hCG by Nichols versus values of ~4 to ~760 mIU/mL by DPC Assay. Thus this **Nichols H-hCG Assay** yielded values in ng/ml that correlated well [i.e., gave correlation factor r= 0.935 (and P-Value < 0.001)] with the DPC values, allowing for unit conversion from the predicate DPC units [i.e., mIU]. The NID assay gave ng units of H-hCG by way of a Linear Regression Expression: **Y(DPC's) = + 28.32X(NID's) -5.36** and yielded an acceptable determined correlation factor: r = **0.935,** and **P-value < 0.001** (using n = 61 critical pregnancy patient determination).

12.8.1.c. Traceability (controls, calibrators, or method):

The Nichols Advantage H-hCG assay is designed specifically to detect the present of Hyperglycosylated Human Chorionic Gonadotropin in both serum and urine. The Nichols Advantage H-hCG assay utilizes the monoclonal antibodies developed at Columbia University specific against to the isoforms of H-hCG. One of the antibodies (B152 obtained from Columbia University directed against H-hCG) is biotin labeled (US Patent #:5395938) and used as a capture antibody. The other antibody, H-hCG non-specific (B207 also obtained from Columbia University) is labeled with acridinium ester (ACR, US Patent #:5284952) and used for detection. Where B152 used as capture antibody is specific to the carbohydrate isoforms (H-hCG), the B207 antibody is against general hCG β for detection. During assay, the serum or urine sample is added to a cuvette well within the Nichols Advantage Specialty System followed by the addition of the biotinylated-B152 anti-H-hCG antibodies and streptavidin-coated magnetic particles (Dynabeads®) obtained from Dynal Biotech. See Cross-Reactivity section below.

12.8.1.d. Detection limit:

In a detection limit study using H-hCG Nichols Advantage assay, N=81, non-pregnant apparently health female subjects, the detection levels of H-hCG for all subjects were under 0.3 ng/ml, and 95% of non pregnant subjects were below the detection level (0.2 ng/ml). None of the samples exceed a level of 1.0 H-hCG ng/ml in serum among normal non-pregnant subjects. The analytical sensitivity calculated from the Nichols Advantage® H-hCG Assay was no greater than 110% of the analytical sensitivity of the IMMULITE hGC 2000 analytical sensitivity, which had an accepted hCG analytical sensitivity of 1.0 mIU/mL. Therefore, Positive results from serum should only be reported out for serum H-hCG results equal to or greater than 1.0 ng/ml serum with the numerical. Positive results from urinary analysis may only be reported as Qualitatively Positive if the

analytical results are equal or greater than 1.0 ng/ml urine, but without the numeric results being posted (i.e., a qualitative result of Positive without any numerical value assigned).

12.8.1.e. Analytical Specificity:

For analytical specificity, this Nichols H-hCG Assay was evaluated for cross-reactivity (CR) against 5 mIU TSH/mL, 80 IU LH/mL, 20 IU FSH/mL, 25 ng hPL/dL and 10 ng hGH/mL. No detectable cross-reactivity was observed. This assay was tested for cross-reactivity with various forms of hCG provided by Columbia University or from Sigma Chemical Co., and the results shown in the table below were obtained:

Source	h CG Hormone	Lot No.	Concentration	Cross-reactivity (%)
Sigma (P/N C6322)	hCG, recombinant	081K10-098	2000 IU/mL	< 1
Columbia University	Non-nicked hCG*	-814	10.6 uM	4.5
	Non-nicked Free Beta hCG	-931	2.1 uM	1.0
	Nicked hCG**	-813	137 nM	5.4
	Nicked Free Beta hCG***	-841	20 nM	1.5

* Non-nicked hCG (regular hCG,MW~36kDa) contains α-subunit with 92 and β-subunits with 145 amino acid residue polypeptide; Non-nicked. **Nicked hCG (MW~36.5kDa) contains α-subunit with 92 and β-subunits with 145 amino acid residue polypeptide and with β-subunit polypeptide nicked/cut at β47-48, β43-44 or β44-45; ***Nicked, Free Beta hCG (MW~36.5kDa) contains only β-subunits polypeptide nicked/cut at b47-48, b43-44 or b44-45; these isoforms of hCG were obtained from Columbia University isolated from human body fluids.

12.8.1.f. Assay cut-off:

The minimum detectable concentration (MDC), or analytical sensitivity, of the Nichols Advantage® H-hCG Assay was determined using n = 81 non-pregnant apparently health female subjects. In this study, the detection levels of H-hCG for all subjects were under 0.3 ng/ml, and 95% of non-pregnant subjects were below the detection level (0.2 ng/ml), as summarized above in Section 1.d and the table below. None of the samples exceed a level of 1.0 H-hCG ng/ml in serum among normal non-pregnant subjects. This table depicts the Nichols Advantage® H-hCG Assay results:

INTERPRETATION OF RESULTS

Nichols Advantage® H-hCG Assay	
Result	**Interpretation**
Greater than or equal to 1.0 ng/mL both in serum and urine	Positive for pregnancy
Less than 1.0ng/mL both in serum and urine	Negative for pregnancy

The analytical sensitivity (Limit Of Detection, LOD) was determined by reading the +2SD response from n=20 replicate measurements of the zero standard from the stored master curve from several runs and systems. The analytical sensitivity for this assay was estimated to be at or below 0.2 ng/mL, while the Critical cut-off for pregnancy determination was found to be 1.0 ng/mL. Each laboratory should determine their own lower limit of detection based on their facilities' procedures. The relative sensitivity between the Nichols Advantage H-hCG Assay with the DPC Immulite predicate assay was found to be 100.0% in serum and 99.0% in urine.

Again, we note that Positive results from serum should only be reported out for serum H-hCG results equal to or greater than 1.0 ng/ml serum with the numerical. Positive results from urinary analysis may only be reported as Qualitatively Positive if the analytical results are equal or greater than 1.0 ng/ml urine, but without the numeric results being posted (i.e., a qualitative result of Positive without any numerical value assigned).

12.8.1.g. Reproducibility

The Within-Run and Total imprecision of the Nichols Advantage H-hCG assay was calculated using the NCCLS EP5-A method (Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline). Serum pools and controls were tested in duplicate in two runs per day over 6 days. At a dose greater than 10 ng H-hCG/mL the Within-Run imprecision was not greater than 5% and the Total imprecision was not greater than 10%. The study was performed on five Nichols Advantage Specialty Systems.

12.8.1.h. High Dose Hook Effect Level

The high dose hook effect for the Nichols Advantage H-hCG Assay was determined to be greater than 31,000 ng/mL. Samples containing H-hCG values up to 31,000 ng/mL will read greater than the dynamic range.

12.8.2. Comparison studies:

12.8.2.a. Method and Matrix Comparisons with Predicate Device

The Nichols Advantage H-hCG assay was compared to the DPC IMMULITE 2000 hCG assay. A total of 1436 sample points were collected, including serum of pregnant (n=479, 1st trimester n=378, 2nd trimester n= 101) and non-pregnant (n=180); urine of pregnant (n=632, 1st trimester n=374, 2nd trimester n=258) and non-pregnant (n= 145) for the comparison. All the samples were assayed by both procedures following the manufacturers' directions and without modifications. Using the positive cut-off value for detection of pregnancy by the Nichols Advantage H-hCG assay (H-hCG >1.0 ng/ml) determined by the conversion of DPC's international units from mIU/ml to the NID's units of ng H-hCG/ml serum, the relative sensitivity between the Nichols Advantage H-hCG assay with the DPC predicate device was 100.0% in serum and 99.0% in urine.

METHOD COMPARISON (SERUM) DPC vs. NID

'n =659

	DPC		
NID	Positive	Negative	Total
Positive	473	6	479
Negative	0	180	180
Total	473	186	659
		95% CI	
Concordance	99.1%	98.4%	-100%
Percentage agreement positive	100.%	99.1%-	-100%
Percentage Agreement negative	96.8%	93.4%	-98.6%

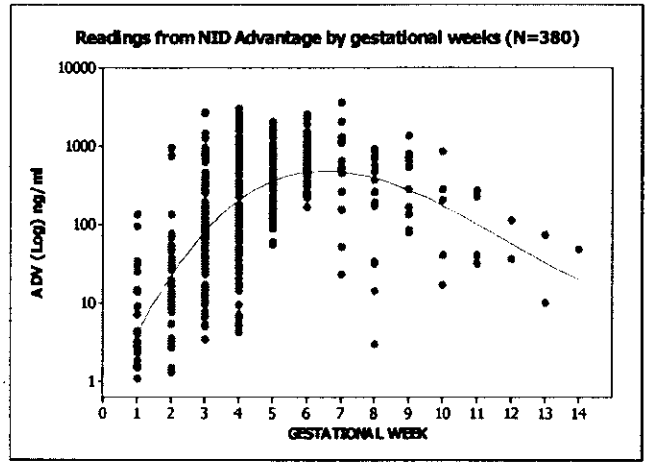
METHOD COMPARISON (URINE) DPC vs. NID

'n =777

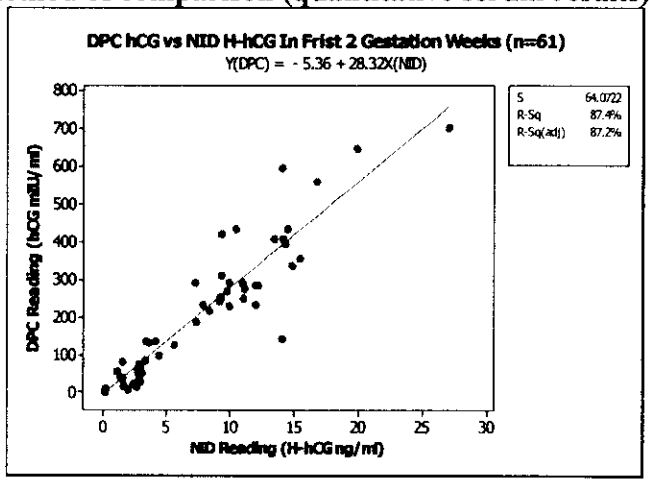
	DPC		
NID	Positive	Negative	Total
Positive	616	16	632
Negative	6	139	145
Total	622	155	777
		95% CI	
Concordance	97.2%	97.93%	-98.4%
Percentage agreement positive	99.0%	97.9%	-99.6%
Percentage Agreement negative	89.6%	83.9%	-93.6%

Note: For n = 61 data pairs (from 357) with specific gestation equal or less than 2 weeks, results by both methods gave correlation readings of: ***Y[DPC] = - 5.36 + 28.32 X[NID]*** and showed correlation value of $r = 0.935$, & P-Value < 0.001 as shown in graph 2 below:

GRAPH 1: Expected H-hCG values determined from serum during the 1st trimester of pregnancy



GRAPH 2: Method of comparison (quantitative serum results):



12.8.3. Expected values/Reference range:

12.8.3.a. DECISION THRESHOLD

Nichols Institute Diagnostics recommends that each laboratory establish its own expected values for the population they serve. To establish an expected reference range, the levels of H-hCG were respectively determined in serum samples (n=178) and random urine samples (n=85) apparently healthy and non-pregnant, ambulatory, free-living, southern California community-dwelling adult women. The women who donated serum ranged in age from 17 to 64; those who donated urine ranged in age from 17 to 71. Decision threshold (cut-off point) for this Nichols H-hCG assay was assigned as: Negative/Quantitative for less than 1.0 ng H-hCG/mL in serum anNegative/Qualitative for less than 1.0 ng H-hCG/ml in urine [See Summary Table below].

INTERPRETATION OF RESULTS SUMMARY TABLE

Nichols Advantage® H-hCG Assay	
Result	**Interpretation**
Greater than or equal to 1.0 ng/mL both in serum and urine	Positive for pregnancy
Less than 1.0ng/mL both in serum and urine	Negative for pregnancy

Again, we note that Positive and Numerical results from serum samples should only be reported out for serum H-hCG results equal to or greater than 1.0 ng/ml serum. Positive results from urinary analysis may only be reported as Qualitatively Positive results only if the analytical results are equal or greater than 1.0 ng/ml urine, but without any numeric results being posted (i.e., a qualitative result of Positive without any numerical value assigned).

12.8.3.b. EXPECTED VALUES

Based on its relationship to hCG (see Method Comparison), the similar pattern of reference ranges as follows are expected. In a study using H-hCG Nichols Advantage assay, n=81, non-pregnant apparently health female subjects, the detection levels of H-hCG are all under 0.3 ng/ml, and 95% of non-pregnant subjects were below the detection level (0.2ng/ml), and none of the samples exceed the level of 1ng/ml in serum among normal non pregnant subjects. Based on n=61 women in the gestational period of 0-2 weeks, the decision threshold (cut-off point) for non-pregnant using this Nichols H-hCG assay was determined to be less than 1.0 ng H-hCG/mL in serum and less than 1.0 ng H-hCG/mg creatinine in urine [See Summary Table above], and a "pregnant" result would be at or above these levels.

In summary, a total of 357 first trimester serum samples from apparently healthy pregnant women were tested by using Nichols Advantage H-hCG Assay. The observed results were summarized below (in ng/ml) by gestational weeks (GES-WK) and by gestational age since last menstrual period (LMP). These readings are considered as the guideline only and each laboratory should establish its own reference ranges. Again, we note that Positive and Numerical results from serum samples should only be reported out for serum H-hCG results equal to or greater than 1.0 ng/ml serum. Positive results from urinary analysis may only be reported as Qualitatively Positive results only if the analytical results are equal or greater than 1.0 ng/ml urine, but without any numeric results being posted (i.e., a qualitative result of Positive without any numerical value assigned).

GES-WK.	LMP	N	MEDIAN	CENTRAL. 95% ± 2SD
>0-2	2-4	37	2.9	2.7-13.3
2-3	4-5	55	14.5	11.8-28.9
3-4	5-6	90	73.6	57.4-149.5
4-5	6-7	73	230.1	114.6-435.8
5-6	7-8	47	490.1	369.8-650.4
6-7	8-9	31	585.0	514.9-1054.3
7-12	9-14	24	101.7	42.2-297.9

12.8.3.c. PARALLELISM

Samples with varying concentrations of H-hCG were either manually diluted with Sample Diluent before placing onto the system, or diluted on-board the system. The results demonstrate linearity across the dynamic range of this Nichols Advantage H-hCG immunochemiluminescent assay.

Serum No.	Dilution	Observed (ng/mL)	Expected (ng/mL)	% Recovery
1	Undiluted	12.2		
	1:2	6.7	6.1	110
	1:4	3.3	3.1	106
2	Undiluted	70.1		
	1:2	35.2	35.1	100
	1:4	19.1	17.5	109
	1:8	9.0	8.8	102
3	Undiluted	135.6		
	1:2	69.5	67.8	103
	1:4	37.1	33.9	109
	1:8	19.6	17.0	115

12.8.3.d. RECOVERY

Three sets of a high and a low/normal serum samples were mixed in 2:1, 1:1 and 1:2 ratios and assayed. The recoveries were determined from the undiluted results. The results demonstrate recovery of H-hCG in patients' samples between 89 and 110%.

Serum Sample	Observed(ng/mL)	Expected(ng/mL)	% Recovery
Sample A	135.6		
2 : 1	86.6	97.0	89
1 : 1	75.2	77.7	97
1 : 2	55.6	58.4	95
Sample B	19.8		
Sample C	154.4		
2 : 1	103.0	106.5	97
1 : 1	74.1	82.6	90
1 : 2	55.7	58.6	95
Sample D	10.7		
Sample E	82.9		
2 : 1	60.2	59.1	102
1 : 1	44.8	47.3	95
1 : 2	33.9	35.4	96
Sample F	11.6		

12.9. Performance Characteristics - Summary

Table of Methods Comparisons – for Recovery, Hook Dose & Cross-Reactivity*

FEATURE	DPC IMMULITE hCG Immunoassay*		Nichols Advantage H-hCG Assay*	
Within-Run	Not greater than 7% at dose greater than 6.5 mIU/mL Serum		Not greater than 5% at a dose greater than 10 ng/mL Serum	
Total	Not greater than 8% at dose greater than 6.5 mIU/mL Serum		Not greater than 10% at a dose greater than 10 ng/mL Serum	
Recovery	100% – 112%		89% – 110%	
Parallelism	91% to 98%		86% - 115%	
High Dose Hook Effect	None up to 2,000,000 mIU/mL		None up to 31,000 ng/mL	
Cross-Reactivity	**DPC IMMULITE hCG Immunoassay***		**Nichols Advantage H-hCG Assay***	
Cross-Reactant	Quantity Spiked (ng/mL)	Cross-Reactivity	Quantity Spiked (ng/mL)	Cross-Reactivity
FSH	26.8	ND	10000	0.0%
LH	16.5	ND	10000	0.1%
TSH	860	ND	10000	0.0%

* Table 22a shows the performance characteristics in parallel between DPC and NID assays where DPC's readings were in mIU/ml and NID readings were in ng/ml except cross reactivity results in ng/ml as substances were spiked.

** FSH Unit/Mass conversion factor: 2735 IU/mg
LH Unit/Mass conversion factor: 10,000 IU/mg
TSH Unit/Mass conversion factor: 6.5 IU/mg

Table of Methods Comparisons – for Both Serum & Urine re: Positives & Negatives**

Method Comparison**	
Serum Sample Size:	659 (pregnant and non pregnant)
Range of Results:	DPC IMMULITE hCG Immunoassy: < 1 mIU hCG/mL to 365,224 mIU hCG/mL, serum. Nichols Advantage H-hCG Assay: < 1 ng H-hCG/mL to 3616 ng H-hCG/mL, serum.
Concordance:	99.1%
Percent Agreement Positive:	100%
Percent Agreement Negative:	96.8%
Urine Sample Size:	777(pregnant and non pregnant)
Range of Results:	DPC IMMULITE hCG Immunoassy: < 1 mIU hCG/mL to 493,194 mIU hCG/mL, urine. Nichols Advantage H-hCG Assay: < 1 ng H-hCG/ml to 1,689 ng H-hCG/ml, urine.
Concordance:	97.2%
Percent Agreement Positive:	99.0%
Percent Agreement Negative:	89.7%

12.10. Conclusions

Based upon the information provided, the **Nichols Advantage® H-hCG Assay** [quantitative with serum and qualitative with urine] has been found to be substantially equivalent or **SE** to the DPC predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 17 2004

Nichols Institute Diagnostics
c/o Alfredo Quattrone, Ph.D.
California Department of Health
Food and Drug Branch
1500 Capitol Avenue
Mailstop 7602
Sacramento, CA 95814

Re: k042676
Trade/Device Name: Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay
Regulation Number: 21 CFR 862.1155
Regulation Name: Human Chorionic gonadotropin (HCG) test system
Regulatory Class: Class II
Product Code: DHA, JIT, JJX
Dated: October 22, 2004
Received: October 26, 2004

Dear Dr. Quattrone:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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) that do not require approval of a premarket approval application (PMA). 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 (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer 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,

Cornelia B. Rooks

Cornelia B. Rooks, MA
Acting Director
Division of Chemistry and Toxicology
Office of In Vitro Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE

510(k) Number: **K042676**

Device Name: **Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay**

Indications For Use Statement: The Nichols Advantage Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay (or simply: **Nichols Advantage® H-hCG Assay**) is intended for use with the Nichols Advantage® Specialty System for the quantitative measurement of hyperglycosylated human chorionic gonadotropin (H-hCG), a placental hormone in human serum, or for the qualitative determination of H-hCG in urine as an aid in the detection of pregnancy. These diagnoses should be made with appropriate additional clinical evidence. Clinical considerations and professional judgment should be applied to any test device result as with this Nichols H-hCG chemiluminescent immunoassay.

The Nichols Advantage® H-hCG Assay is used in conjunction with two H-hCG calibrators which are used to calibrate the assay and are provided separately to the reagent cartridge. The control is used for the monitoring of the accuracy and precision of the Nichols Advantage H-hCG Assay and successful calibration is confirmed using three H-hCG controls also provided separately to the calibrators and reagent cartridge.

Prescription Use ___√___ AND/OR Over-The-Counter use _____.

(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIDE)

Carol C. Benson

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

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