510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k042676

B. Purpose for Submission:

New device

C. Measurand:

Human chorionic gonadotropin

D. Type of Test:

Quantitative and qualitative, Immunochemiluminometric assay

E. Applicant:

Nichols Institute Diagnostics

F. Proprietary and Established Names:

Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay; Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin Calibrators; and Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin Controls

G. Regulatory Information:

1. Regulation section:

    21 CFR 862.1155, Human chorionic gonadotropin (HCG) test system
    21 CFR 862.1150, Calibrator
    21 CFR 862.1660, Quality control material (assayed and unassayed)

2. Classification:

    Class II (hCG test system and calibrator), Class I (quality control material)

3. Product code:

   DHA (hCG test system), JIT (calibrator), JJX (quality control material)

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   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 Hyperglycosylated Human Chorionic Gonadotropin Calibrators are intended for adjustment of the stored curve for Nichols Advantage® Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Assay.

   The Nichols Advantage Hyperglycosylated Human Chorionic Gonadotropin (H-hCG) Controls are intended for use as an assayed quality control solution to monitor the accuracy and precision of the Nichols Advantage H-hCG Immunoassay.

2. Indication(s) for 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 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.

3. Special conditions for use statement(s):

This device is for clinical laboratory use only and for prescription use only.

4. Special instrument requirements:

Nichols Advantage® Specialty System

I. Device Description:

The Nichols Advantage H-hCG Assay is composed of the following materials:

- One cartridge with the following reagents sufficient for 100 tests: one vial containing streptavidin-coated magnetic particles in PBS buffer and preservatives
- One vial containing acridinium ester-labeled mouse anti-H-hCG antibody solution
- One vial containing biotinylated rabbit anti-mouse anti-H-hCG antibody solution
- One vial of heat-treated mouse serum with preservative
- Diluent
- Assay Buffer
- One lot specific H-hCG Master Curve Bar Code Card

Calibrators and controls are required but are sold separately. The two calibrators are each supplied in four 1.0 mL vials, each containing lyophilized buffered protein solution with preservative. The target concentrations are as follows: Cal A (1.0 ng/mL) and Cal B (100ng/mL). The three controls are each supplied in four 1.0 mL vials, each containing H-hCG in a lyophilized buffered protein solution with preservative. The target concentrations are as follows: Level 1 (2.0 ng/mL), Level 2 (20 ng/mL), and Level 3 (200 ng/mL).

The calibrators and controls contain materials of human origin which have been tested using FDA approved methods and have been found negative for antibodies to Human Immunodeficiency Virus (HIV I and HIV II) and to Hepatitis C Virus (HCV), as well as for Hepatitis B surface antigen (HBsAg).

J. Substantial Equivalence Information:

1. Predicate device name(s):

IMMULITE® hCG Assay

2. Predicate 510(k) number(s):

   k990222

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Antibody Recognition	Specific antibodies that bind isoforms of hCG	Same
Sample Type	Human serum or urine	Same
Analysis Technology	Utilizes chemiluminescent technology for quantitation with assay incubated to 37°C.	Same

Differences		
Item	Device	Predicate
Capture/Detection Material	Biotinylated and acridinium ester-labeled mouse monoclonal anti-H-hCG antibodies coated on magnetic particles	Monoclonal antibody coated polystyrene bead
Sample Volume	15 microliters	5 microliters
Standardization	C5 antigen of Elliott et al.	WHO 3rd I.S.
Reporting Unit	ng/ml [based on Mass units of ng per ml serum]	mIU/ml [based on milli-International Units]

K. Standard/Guidance Document Referenced (if applicable):

NCCLS EP5-A

L. Test Principle:

The Nichols Advantage H-hCG Assay is a two-step, two-site immunochemiluminometric assay. Sample, biotinylated-B152 anti-H-hCG antibodies, and streptavidin-coated magnetic particles are allowed to incubate. Unbound assay components and other sample constituents are separated from the complex bound to the magnetic particles by aspiration of the reaction mixture and subsequent washing. Acridinium-labeled anti-H-hCG antibodies are added, creating the sandwich complex. The magnetic particles are washed and transported into the system luminometer, which injects Triggers 1 and 2, initiating the chemiluminescent reaction. The luminometer quantitates the light and expresses it as relative light unit (RLU). The signal is directly proportional to the concentration of H-hCG in the sample. The

quantity of H-hCG in the sample is determined by comparing the signal of the sample to that of a known standard.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

    a. *Precision/Reproducibility:*

    To evaluate precision, the within-run and total precision 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. The study used five Nichols Advantage Specialty Systems. The results were as follows:

Sample	Mean (ng/mL)	Within-Run		Total Precision	
		SD	%CV	SD	%CV
1	3.0	0.10	3.4	0.16	5.4
2	9.0	0.16	1.8	0.45	5.0
3	27.7	0.92	3.3	1.38	5.0
4	44.8	2.36	5.3	2.82	6.3
5	173	5.88	3.4	12.75	7.4

    b. *Linearity/assay reportable range:*

    The highest reportable value without dilution is the value of the highest point on the Master Curve (300 ng/mL). The following studies were performed to support linearity.

    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 observed and corrected results are presented. The results demonstrate linearity across the dynamic range of this Nichols Advantage H-hCG Assay.

Serum Sample	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

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 102%.

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		

Dilution and recovery of a pooled serum sample at 285 ng/mL H-hCG was performed and yielded an average recovery of 103.8%. See the table below:

Sample 285.5 ng/mL	Dose (ng/mL)	Corrected dose (ng/mL)	% Recovery
1 : 2	148.7	297.4	104.2
1 : 4	73.4	293.6	102.8
1 : 8	37.0	296.0	103.7
1:10	29.8	298.0	104.4

The high dose hook effect for the Nichols Advantage H-hCG Assay was determined to be greater than 31,000 ng/mL. Linear regression analysis within the dynamic range (up to 300 ng/mL) yielded an R-square value of 0.998647. See graph below.

Linear Regression Analysis (Within Dynamic Range)
Response RLU Unit and Regression Plot