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

A. 510(k) Number:

k103574

B. Purpose for Submission:

New device

C. Measurand:

Human chorionic gonadotropin (hCG) in human urine

D. Type of Test:

Qualitative immunochromatographic assay

E. Applicant:

Zhejiang Orient Gene Biotech, Co.,Ltd.

F. Proprietary and Established Names:

Pregnancy One Step Rapid Test (Strip)

Pregnancy One Step Rapid Test (Cassette)

Pregnancy One Step Rapid Test (Midstream)

G. Regulatory Information:

1. Regulation section:

   21 CFR§ 862.1155, Human chorionic gonadotropin (HCG) test system

2. Classification:

   II

3. Product code:

   LCX

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See below.

2. Indication(s) for use:

   The Pregnancy One Step Rapid Test Strip is an in vitro diagnostic visual qualitative immunochromatographic assay designed for the rapid determination of human chorionic gonadotropin (hCG) in urine to aid in the early detection of pregnancy. For professional use only.

   The Pregnancy One Step Rapid Test Cassette is an in vitro diagnostic visual qualitative immunochromatographic assay designed for the rapid determination of human chorionic gonadotropin (hCG) in urine to aid in the early detection of pregnancy. For professional use only.

   The Pregnancy One Step Rapid Midstream Test is an in vitro diagnostic visual qualitative immunochromatographic assay designed for the rapid determination of human chorionic gonadotropin (hCG) in urine to aid in the early detection of pregnancy. For OTC self-testing use.

3. Special conditions for use statement(s):

   Test strip and cassette formats are for prescription use.

   Midstream format is for over-the-counter (OTC) use.

4. Special instrument requirements:

   None

I. Device Description:

The Pregnancy One Step Rapid Test is a rapid sandwich immunoassay device designed for the qualitative determination of human chorionic gonadotropin (hCG) concentration in human urine samples, as an aid in the early detection of pregnancy. The test is available in three formats: strip, cassette, and midstream. The midstream format is intended for OTC use. The cassette and strip formats are intended for prescription use. All three configurations have the same membrane format, reagents, and flow characteristics. Devices are packaged one device per pouch with 2 devices

per kit.

J. Substantial Equivalence Information:

1 and 2. Predicate device name(s):

Name	Format	510k
Acon Combo Pregnancy	Cassette	k993065
Acon hCG One Step Pregnancy Test Strip	Strip, Cassette	k993317
Acon Spectrum Midstream	Midstream cassette	k042151

3. Comparison with predicate:

Similarities		
Item	Device	Predicate device
Intended Use	The Pregnancy One Step Rapid Test is an in vitro diagnostic visual qualitative immunochromatographic assay designed for the rapid determination of human chorionic gonadotropin (hCG) to aid in the detection of pregnancy.	Same
Sensitivity	25 IU/mL	Same
Storage	2 - 30ºC	Same
Principle	Sandwich Immunochromatographic Assay	Same

Differences		
Item	Device	Predicate device
Users	Prescription and OTC	Prescription
Specimen	Urine	Urine, serum
Read Time	5 Minutes	3 minutes
Test Line	Particle Membrane Immunoassay	Colloidal Gold
Formats	Strip, cassette, midstream	Strip and midstream

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

Guidance for Industry and FDA Reviewers/Staff: *FDA Guidance for Over-the-Counter (OTC) Human Chorionic Gonadotropin (hCG) 510(k)s*

CLSI EP7-A2; *Interference Testing in Clinical Chemistry*

L. Test Principle:

The Pregnancy One Step Rapid Test is a qualitative, solid phase, two-site sandwich immunoassay for the detection of human chorionic gonadotropin (hCG) in urine. The membrane is pre-coated with monoclonal anti-hCG antibodies on the test band region and anti-mouse antibodies on the control band region. During testing, the urine sample reacts with the dye conjugate (mouse anti-hCG antibody-colloidal gold conjugate) which has been pre-coated on the test strip. The mixture then migrates upward on the membrane chromatographically by capillary action to react with anti-hCG antibodies on the membrane and generate a red band. Presence of the red band indicates a positive result, while its absence indicates a negative result. Regardless of the presence of hCG, as the mixture continues to migrate across the membrane to the immobilized goat anti-mouse region, a red band at the control band region will always appear. The presence of this red band serves as verification for sufficient sample volume and proper flow and as a control for the reagents.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:
Reproducibility of each device type was evaluated at three sites by three users per site. Each device format was evaluated—test strip, cassette, and midstream. Testing was performed by spiking negative urine samples with purified hCG, traceable to WHO International 4th Standard, to 15 mIU/mL, 20 mIU/mL, 25 mIU/mL, 30 mIU/mL, 35 IU/mL of hCG over 3 days. hCG concentrations were confirmed by a FDA cleared commercially available chemiluminescent immunoassay. Healthcare professionals (HCP) performed testing on the cassette and test strip. Lay users performed the midstream testing. All samples were blinded to both the HCPs and lay users. Inter-site and day-to-day precision by device format results are shown below:

Test Strip

		Site						Total	
		1		**2**		**3**			
		+	-	+	-	+	-	+	-
HCG concentration (mIU/mL)	**15**	0	27	0	27	0	27	0	81
	20	1	26	0	27	1	26	2	79
	25	13	14	12	15	14	13	39	42
	30	26	1	27	0	27	0	80	1
	35	27	0	27	0	27	0	81	0

Cassette

		Site						Total	
		1		**2**		**3**			
		+	-	+	-	+	-	+	-
HCG concentration (mIU/mL)	**15**	0	27	0	27	0	27	0	81
	20	0	27	1	26	2	25	3	78
	25	11	16	13	14	13	14	37	44
	30	26	1	27	0	27	0	80	1
	35	27	0	27	0	27	0	81	0

Midstream

		Site						Total	
		1		**2**		**3**			
		+	-	+	-	+	-	+	-
HCG concentration (mIU/mL)	**15**	0	27	0	27	0	27	0	81
	20	0	27	2	25	0	27	2	79
	25	12	15	15	12	11	16	38	43
	30	27	0	26	1	26	1	79	2
	35	27	0	27	0	27	0	81	0

Precision data was also compared among the three formats e.g., strip, cassette, and midstream, to demonstrate that the performance of each test format, was similar across all test sites. Results are summarized below:

		Configuration						Total	
		Test Strip		**Cassette**		**Midstream**			
		+	-	+	-	+	-	+	-
HCG concentration (mIU/mL)	**15**	0	81	0	81	0	81	0	243
	20	2	79	3	78	2	79	7	236
	25	39	42	37	44	38	43	114	129
	30	80	1	80	1	79	2	239	4
	35	81	0	81	0	81	0	234	0

b. Linearity/assay reportable range:

Not applicable. This is a qualitative device.

Hook effect studies were performed on three lots of test strips at hCG concentrations of 50, 100, 200, 300, 500 IU/mL of hCG. No hook effect was observed at < 300 IU/mL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The devices are traceable to the WHO 4th International Standard for hCG.

Closed pouch real time stability studies were performed separately on three lots of each format—test strips, cassette and midstream. The devices were stored at 2-8°C, and 25-30°C for 18 months. Samples were tested were tested every 2 months with the WHO 4th International Standard for hCG at 4 concentrations around the cutoff. Based on these studies, closed pouch stability is 18 months when stored at 2-30°C.

Open pouch studies were performed over 5 days at 25-30°C and ≥ 85% relative humidity for various concentrations of hCG. Based on these studies, the device was stable for one day once opened, however, labeling recommends that testing take place immediately after opening the pouch.

d. Detection limit:

See cutoff studies M.1.f.

e. Analytical specificity:

An interference study was carried out with two lots of the test strips on urine samples containing 5 mIU/mL and 50 mIU/mL of hCG. These pools were further spiked with 2 concentrations of potential interfering substances at therapeutic and toxic concentrations following CLSI-EP7A. 10 replicates of each interferent at each hCG concentration were analyzed for each lot (n=20). Interference was defined as ≥ 95% agreement with the control samples. Complete agreement (100%) was observed for the control samples at 5 mIU/mL and 50 mIU/mL of hCG. The highest interferent concentration demonstrating tested, showing no interference is summarized below:

Acetaminophen	21.1 mg/dL
Acetylsalicylic acid	64.8 mg/dL
Ampicillin	5.9 mg/dL
Ascorbic acid	6340 mcg/dL
Atropine	926.1 mcg/dL
Caffeine	6214.4 mcg/dL
Tetracycline	1777.6 mcg/dL
Bilirubin	18.71 mg/dL
Hemoglobin	2 g/L
Glucose	1000 mg/dL
Total Protein	120 g/L
Albumin	60 g/L

A cross-reactivity study was carried out by adding known amounts of potential cross reactants of LH, FSH, and TSH to a total of 90 negative urine samples to evaluate the test result lines of 3 lots of test strips. The cross-reactivity results are shown below:

	Lot I	Lot II	Lot III
LH 300 mIU/mL	None	None	None
FSH 1000 mIU/mL	None	None	None
TSH 1000 mIU/mL	None	None	None

No cross-reactivity was observed for urine samples up to the following concentrations: LH = 300 mIU/mL, FSH = 1000 mIU/mL, and TSH = 1000 mIU/mL.

Cross-reactivity studies to β-core hCG were also performed using 10 strips from 3 lots of test strips (n=30). 0.5, 10 and 200 mcg/mL of β-core hCG were added to samples containing 5 mIU/mL and 50 mIU/mL of hCG. Results are summarized below and expressed as the number of positive samples per lot number for each hCG concentration tested.

β-core hCG Concentrations

	0.5 mic/mL			**10 mic/mL**			**200 mic/mL**		
hCG	**Lot 1**	**Lot 2**	**Lot 3**	**Lot 1**	**Lot 2**	**Lot 3**	**Lot 1**	**Lot 2**	**Lot 3**
5 mIU/L	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/10
50 mIU/L	10/10	10/10	10/10	10/10	10/10	10/10	10/10	10/10	10/10

There was no cross-reactivity with β-core hCG up to 200 mcg/mL

The effects of pH and specific gravity were evaluated by testing 10 replicates of urine samples spiked with hCG at pH 2-9 and specific gravity of 1.003-1.030. No interference was observed for pH or specific gravity. However, labeling states that low concentrations of hCG may not be detected in very dilute urine and, if pregnancy is suspected, repeat testing should be performed after 48 hours.

f. Assay cut-off:

To confirm the cut-off with the intended use population, studies were performed separately from the precision tests for the test strip, cassette, cartridge and midstream formats. The sponsor followed CLSI EP12-A and identified the cut-off as 25 mIU/mL. Negative human urine samples were spiked with purified hCG traceable to the WHO International 4th Standard to 15 mIU/mL (-40% cutoff), 20 mIU/mL (-20% cutoff), 25 mIU/mL, 30 mIU/mL (+20% cutoff), 35 mIU/mL (+40% cutoff). hCG concentrations were confirmed by a commercially available chemiluminescent method. Studies were performed at 3 point-of-care (POC) sites by 3 healthcare professionals (HCP) and 3 lay users at each site. All samples were masked prior to analysis. HCPs performed the testing on the test strip and cassette

formats. Lay users performed testing midstream format and collected the remaining sample in a cup for additional testing. Three lots of test strips, cassettes and midstream devices were used across all sites. Results are expressed as the number of positive samples to the total number of samples analyzed. See below:

	Strip	Cassette	Midstream
15 mIU/mL (-40% cutoff)	0/81	0/81	0/81
20 mIU/mL (-20% cutoff)	1/81	2/81	1/81
25 mIU/mL (cutoff)	39/81	37/81	38/81
30 mIU/mL (+20% cutoff)	80/81	80/81	79/81
35 mIU/mL (+40% cutoff)	81/81	81/81	81/81

2. Comparison studies:

a. Method comparison with predicate device:

Comparison studies between the test strip, cassette and predicate device were conducted by one healthcare professional each at 3 point of care sites on 3 lots of each device format. Each site collected 50-60 samples (N=167). The samples were collected from women who fit the following categories: childbearing age, peri-menopausal, suspected of being pregnant, e.g. within days of missing the expected menses, within the first 30 days of pregnancy, and the first trimester of pregnancy. All samples were masked prior to analysis. Users performed the testing according to the labeling.

Results are summarized below:

		Predicate device		
		Positive	**Negative**	**Total Agreement**
Test Strip n= 167	**Positive**	72	2	
	Negative	3	90	
	Total	75	92	97.0 %

		Predicate device		
		Positive	**Negative**	**Total Agreement**
Cassette n= 167	**Positive**	72	1	
	Negative	3	91	
	Total	75	92	97.6 %

A lay user study was performed using the midstream format of the Orient

Gene Pregnancy HCG Test. Lay users were randomly recruited from the intended use population and did not include healthcare professionals, or laboratorians. Evaluation took place at 3 sites with three lots of devices. 15-20 individuals per site were enrolled in the study (N=56). All were suspected, but not confirmed to be pregnant. Each lay user performed the testing unassisted according to the labeling. In addition to midstream testing, the participants collected their sample in a cup for subsequent blinded testing by healthcare professionals with the Orient Gene Pregnancy HCG test strip format and the predicate device.

		HCP Test strip		
		Positive	**Negative**	**Total Agreement**
Midstream Lay user n= 56	**Positive**	18	2	
	Negative	1	35	
	Total	19	37	94.6%

		Predicate device		
		Positive	**Negative**	**Total Agreement**
Midstream Lay user n= 56	**Positive**	20	0	
	Negative	1	35	
	Total	21	35	98.8%

b. Matrix comparison:

Not applicable. The device is for urine only.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Each lay user was given a questionnaire to assess the readability of the labeling. The results of the questionnaire reflected that the consumers found the test easy to use and that they did not have trouble understanding the labeling and interpreting the results.

4. Clinical cut-off**:**

   Not applicable.

5. Expected values/Reference range:

   Negative results are expected in healthy non-pregnant women. Healthy pregnant women have hCG present in their urine. The amount of hCG will vary greatly with gestational age and between individuals. The test can be used as early as the first day of the missed period.

   A toll free telephone number with hours of operation has been provided in the labeling for technical assistance.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.