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

A. 510(k) Number:

k081150

B. Purpose for Submission:

New device

C. Measurand:

Human Chorionic Gonadotrophin (hCG)

D. Type of Test:

Qualitative chromatographic immunoassay

E. Applicant:

Turklab Medical Devices Inc.

F. Proprietary and Established Names:

Rapidan Optima Early Urine Pregnancy Test
Toyo Pregnancy Urine Test

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LCX, JHI	Class II	21 CFR 862.1155, Human Chorionic Gonadotropin (HCG) test system	75 Clinical Chemistry (CH)

H. Intended Use:

1. Intended use(s):

   See indication for use below

2. Indication(s) for use:

Rapidan Optima Early One Step hCG Urine Pregnancy Test is an *in-vitro* diagnostic test for qualitative determination of human chorionic gonadotrophin (hCG) in human urine. It is intended for over the counter use to detect elevated (over the cut-off value of 20 IU/L) levels of human chorionic gonadotrophin (hCG) in human urine to aid in the detection of pregnancy.

Toyo One Step hCG Urine Pregnancy Test is an *in-vitro* diagnostic test for qualitative determination of human chorionic gonadotrophin (hCG) in human urine. It is intended for over the counter use and for professional / laboratory use to detect elevated (over the cut-off value of 25 IU/L) levels of human chorionic gonadotrophin (hCG) in human urine to aid in the detection of pregnancy. Toyo Pregnancy Test has two formats, a cassette and a test strip format.

3. Special conditions for use statement(s):

Rapidan Optima Early Urine Pregnancy Test is for over-the-counter use.

Toyo Urine Pregnancy Test is for over-the-counter and prescription use.

4. Special instrument requirements:

None

I. Device Description:

The device is a qualitative assay based on immuno-chromatography principle used to detect levels of hCG over the cut-off value (see detection limit, below) of the device.

Toyo Urine Pregnancy Test will be sold in two formats: cassette or test strip. The test strip kit consists of one test device and a package insert. The cassette kit consists of one test device and a disposable plastic dropper, and a package insert. Each test device contains mouse monoclonal anti-α-hCG antibody coated membrane and a pad containing mouse monoclonal anti-β-hCG antibody colloidal gold conjugate. The control antibodies are goat anti-mouse IgG.

Rapidan Optima Early Urine Pregnancy Test will be sold in cassette form only. The cassette kit consists of one test device and a disposable plastic dropper, and a package insert. Each test device contains mouse monoclonal anti-α-hCG antibody coated membrane and a pad containing mouse monoclonal anti-β-hCG antibody colloidal gold conjugate. The control antibodies are goat anti-mouse IgG.

Human source materials was tested by FDA approved methods and found to be negative for the presence of antibodies to HIV-1, HIV-2, HBsAg, and HCV.

J. Substantial Equivalence Information:

1. Predicate device names(s):

   Wondfo One-Step HCG Urine Pregnancy Test

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

   k043443

3. Comparison with predicate:

Similarities and Differences		
Item	Rapidan Optima Early Urine Pregnancy Test (candidate device)	Wondfo One-Step HCG device (predicate device)
Intended Use	Qualitative detection of hCG in human urine for detection of pregnancy for over-the-counter use.	Qualitative detection of hCG in human urine sample for detection of pregnancy for over-the-counter use and professional use.
Test principle	Chromatographic immunoassay	Same
Traceability	4th IS WHO	3rd IS WHO
Specimen	Urine	Same
Cut-offs	20 IU/L	25 IU/L

Similarities and Differences		
Item	Toyo Urine Pregnancy Test (candidate device)	Wondfo One-Step HCG device (predicate device)
Intended Use	Qualitative detection of hCG in human urine for detection of pregnancy for over-the-counter use and professional use.	Same
Test principle	Chromatographic immunoassay	Same
Traceability	4th IS WHO	3rd IS WHO
Specimen	Urine	Same
Cut-offs	25 IU/L	25 IU/L

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

Guidance for Over-the Counter (OTC) Human Chorionic Gonadotropin (HCG) 510(k)s Review Criteria for Assessment of Professional Use Human Chorionic Gonadotropin (HCG) In Vitro Diagnostic Devices (IVDs)

L. Test Principle:

Urine applied at one end of the membrane mobilizes the anti-hCG antibody complex and moves toward the other end of the membrane passing through the immobilized anti-hCG antibody test region and through the antibody recognizing control region. In the presence of hCG, the test line appears on the membrane together with the control line which confirms the antibody complex arrival to the other end of the membrane. For the cassette device, the sample is pipette onto the sample well. For the strip device, the sample is dipped into the sample. The appearance of two color bands, one at the "T" and one at the "C" region means the test is "positive". The appearance of a color band at the "C" region but not at the "T" region means the test is "negative". The appearance of the procedural control "C" band indicates that sufficient sample has been added. If there are no colored bands in the "C" area and "T" area or if there is no color band in "C" area even there is a band in the "T" area; this means "invalid" test result.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:
   A precision study was performed using human urine samples collected from healthy pregnant women and non-pregnant women. Ten different concentrations (0, 10, 20, 25, 40, 50, 10,000, 50,000, 100,000, and 200,000 IU/L) of hCG values were prepared in urine and was tested 100 times by one professional user and one lay user and results were similar. Results are summarized as follows:

   For Rapidan Optima Early Urine Pregnancy Test (Cassette at 20 IU/L):

hCG concentrations	Positive	Negative
0	0	100
10	0	100
20	100	0
25	100	0
40	100	0
50	100	0
10,000	100	0
50,000	100	0
100,000	100	0
200,000	100	0

For Toyo Urine Pregnancy Test:

	(Cassette at 25 IU/L):		(Strip at 25 IU/L):	
hCG concentrations	Positive	Negative	Positive	Negative
0	0	100	0	100
10	0	100	0	100
20	0	100	0	100
25	100	0	100	0
40	100	0	100	0
50	100	0	100	0
10,000	100	0	100	0
50,000	100	0	100	0
100,000	100	0	100	0
200,000	100	0	100	0

b. Linearity/assay reportable range:

Linearity is not applicable since this is a qualitative test.

A hook effect study was performed at levels of 0- 200,000 IU/L (0, 10, 20, 25, 40, 50, 10,000, 50,000, 100,000, and 200,000 IU/L) for each type of tests in combination with the precision study. See 1.a., above. No hook effect was observed up to 200,000 IU/L of hCG value.

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

Rapidan Optima Early Urine Pregnancy Test and Toyo Urine Pregnancy Test are calibrated against reference material traceable to WHO 4th International Standard, 1999 (code: 75/589).

A shelf-life stability test of the devices were performed in real-time and the results showed that the devices were stable for 24 months when stored at 4-30^{o}C (39-86^{o}F).

d. Detection limit:

The detection limit was evaluated by testing 342 urine samples from 19 donors spiked with varying hCG concentration. The hCG concentrations at levels of 0, 5, 10, 15, 20, 25, 30, 40, 50, 100, 200, 400, 800, 1600, 3200, 6400, 12800, and 25600 IU/L were prepared and tested. All samples were tested in duplicates by 2 operators. Results at concentrations near the cutoff are summarized below

hCG IU/L	Rapidan Optima Early Urine Pregnancy- cassette (20 IU cut-off)			Toyo Urine Pregnancy Test – cassette (25 IU cut-off)			Toyo Urine Pregnancy Test - strip (25 IU cut-off)		
	Positive	Negative	Total	Positive	Negative	Total	Positive	Negative	Total
0	0	38	38	0	38	38	0	38	38
5	0	38	38	0	38	38	0	38	38
10	0	38	38	0	38	38	0	38	38
15	0	38	38	0	38	38	0	38	38
20	37	1	38	0	38	38	0	38	38
25	38	0	38	35	3	38	36	2	38
30	38	0	38	38	0	38	38	0	38
40	38	0	38	38	0	38	38	0	38
50	38	0	38	38	0	38	38	0	38
100	38	0	38	38	0	38	38	0	38

e. Analytical specificity:

Cross-reactivity studies were performed to evaluate the interferences from other glycoprotein hormones such as hFSH, hLH, and hTSH. Human FSH (1000 IU/L), hLH (500 IU/L), and hTSH (1000 IU/L) were added to urine samples with varying hCG concentrations (0, 10, 20, 25, 40, 50, 10,000, 50,000, 100,000, 200,000 IU/L) and tested in replicates for both devices (Rapidan Optima Early Urine Pregnancy Test and Toyo Urine Pregnancy Test).

The results of these studies showed that there is no interference at 1000 IU/L hFSH, 500 IU/L hLH, or 1000 IU/L hTSH.

To evaluate the potential for interference by certain exogenous compounds, urine samples with varying hCG concentrations (0, 10, 20, 25, and up to 200,000 IU/L) were spiked with potential interferents and tested. No interferences were observed at the following concentrations tested for both devices (Rapidan Optima Early Urine Pregnancy Test and Toyo Urine Pregnancy Test):

Albumin: 10 mg/L, Ascorbic: 2 g/L, Cellulose: 5 g/L, Glucose: 2000 mg/dL, Haptoglobin: 10 mg/L, Salicylic acid: 1 g/L, Peroxides: 100 mg/L, Hemoglobin: 1 mg/dL, Myoglobin: 10 mg/L, Fruit acid: 4 g/L, Bovine serum: 100 mg/L, Protein: 2000 mg/dL, Cow milk: 100 mg/L, Alcohol: 5 ml/L, Caffeine: 20 mg/dL, Gentisic acid: 20 mg/dL, Atropine: 20 mg/dL.

The sponsor also evaluated the devices and found that samples with pH 4-9 or with densities between 1.003-1.040 were not adversely affected and produced the expected results.

f. Assay cut-off:

The cut-off for a positive test for Rapidan Optima Early Urine Pregnancy Test is 20 IU/L.

The cut-off for a positive test for Toyo Urine Pregnancy Test is 25 IU/L.
See Detection Limit section above.

2. Comparison studies:

a. Method comparison with predicate device:

One hundred urine samples (50 from healthy pregnant and 50 from healthy non-pregnant women, aged 19-46) were collected and split between the candidate devices and the predicate devices (Wondfo One Step hCG urine pregnancy test). Approximately 40% of the samples from pregnant women were collected around the time of missed period. Testing was done at the manufacturing site. Results are summarized below:

Table 1: Comparison between Rapidan Optima Early Urine Pregnancy Test and Wondfo One Step:

		Rapidan Optima Early Urine Pregnancy Test		
		+	-	Total
Wondfo One Step (Predicate device)	+	50	0	50
	-	0	50	50
	Total	50	50	100

Table 2: Comparison between Toyo Urine Pregnancy Test (Cassettes) and Wondfo One Step:

		Toyo Urine Pregnancy Test- Cassettes		
		+	-	Total
Wondfo One Step (Predicate device)	+	50	0	50
	-	0	50	50
	Total	50	50	100

Table 3: Comparison between Toyo Urine Pregnancy Test (Test strips) and Wondfo One Step:

		Toyo Urine Pregnancy Test- Strips		
		+	-	Total
Wondfo One Step (Predicate device)	+	50	0	50
	-	0	50	50
	Total	50	50	100

b. Matrix comparison:

None (This device is only for urine sample).

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):

Three hundred English-speaking women with various education backgrounds participated in the lay user studies using the package insert as a guide. These 300 women donated urine samples and tested only one test device. Separate aliquots of each of the urine samples were masked and provided for testing to the lay user and the professional. The lay users and the professional performed the testing in separate rooms. The professional also tested the predicate device and the results were the same between the candidate device and the predicate device. There were 150 positive samples and 150 negative samples.

An additional study with seventy-five English-speaking women was performed using the package insert as a guide (English version only). The women tested spiked urine samples with hCG concentrations ranging from 0-200 mIU/L, including the cut-offs. Separate aliquots of each of the urine samples were masked and provided for testing to the lay user and the professional. The lay users and the professional performed the testing in separate rooms. The professional also tested the predicate device and the results were the same between the candidate device and the predicate device. There were 39 positive samples and 36 negative samples.

For both studies, there were complete agreement between lay user and professional results for all the 3 devices tested: The Rapidan Optima Early Urine Pregnancy Test (cassette) and the Toyo Urine Pregnancy Test (cassette and test strip formats).

In addition, each patient 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:

The sponsor notes in the package insert that negative results [with this test] are expected in healthy, non-pregnant women. This sponsor's intended use is for this test to detect pregnancy by the first day of the missed period.

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.