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

A. 510(k) Number:

k060128

B. Purpose for Submission:

Modified device

C. Measurand:

Human chorionic gonadotropin

D. Type of Test:

Qualitative

E. Applicant:

Unipath Ltd.

F. Proprietary and Established Names:

Clearblue Easy Digital Pregnancy Test

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1155 – Human chorionic gonadotropin

2. Classification:

   Class II

3. Product code:

   LCX

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   The Clearblue Easy Digital Pregnancy Test is an over-the-counter urine hCG test which is intended for the detection of pregnancy. The test is indicated for use from four days before the expected period.

2. Indication(s) for use:

   The Clearblue Easy Digital Pregnancy Test is an over-the-counter urine hCG test which is intended for the detection of pregnancy. The test is indicated for use from four days before the expected period.

3. Special conditions for use statement(s):

   This device is for over-the-counter use.

4. Special instrument requirements:

   None required

I. Device Description:

The modified Clearblue Easy Digital Pregnancy Test consists of a test chip housed with an absorbent sampler and electronic and optical components in molded case parts. The device is in a ready-to-use format and no longer requires assembly before use. The antibodies in the test stick (i.e., anti-beta hCG, goat anti-rabbit, anti-alpha hCG, and rabbit IgG antibodies) are the same as in the predicate devices.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Clearblue Easy Digital Pregnancy Test

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

   k030659 and k041404

3. Comparison with predicate:

Similarities		
Item	Device	Predicates
Indications for Use	Early detection of	Same

Similarities		
Item	Device	Predicates
Test Principle	pregnancy Sandwich immunochromatographic assay	Same

Differences		
Item	Device	Predicate
Earliest day of use	4 days before expected period	Day of missed period (k030659) 3 days before expected period (k041404)
Device assembly	Integrated test stick and reader in a ready-to-use format	Separate test stick and reader; must be assembled to use device
Sampling time	5 seconds in urine stream 20 seconds in cup	5-7 seconds in urine stream 15 seconds in cup

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

None referenced

L. Test Principle:

Clearblue Easy Digital Pregnancy Test is a sandwich immunoassay employing monoclonal antibodies specific for hCG and uses chromatographic principles to separate bound and free colored label. The reader measures the reflectance of light incident on the test and control lines to determine the test result or if an error has occurred.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The repeatability and reproducibility of the Clearblue Easy Digital Pregnancy Test was challenged over three days and with three different operators who conducted tests on three batches of devices. A negative hCG standard and two positive hCG standards (25 mIU/mL and 50 mIU/mL) were used in the study. One operator tested each of three batches on three consecutive days.

All devices tested with the negative standard gave negative results, and all devices tested with the positive standards gave positive results.

b. Linearity/assay reportable range:

Not applicable

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

The Clearblue Easy Digital Pregnancy Test is standardized against the World Health Organization (W.H.O.) 4th International Standard for chorionic gonadotropin 75/589.

d. Detection limit:

Urine was collected from thirty non-pregnant females. hCG concentration of each sample was determined, and its pH was measured. Each sample was then divided into seven aliquots. Six of these aliquots were spiked with an appropriate amount of hCG standard to produce urine samples having hCG concentrations ranging from 5 mIU/mL to 25 mIU/mL. The unspiked aliquot of each urine sample was also included in the study.

All thirty samples had hCG concentrations <5 mIU/mL and a pH range of 5.0 to 7.5. The results of the sensitivity testing are presented in the table below.

	Number of Positive Results/Total Number Tested			
hCG (mIU/mL)	**Lot 1**	**Lot 2**	**Lot 3**	**Total**
≤5	0/30	0/30	0/30	0/90 = 0%
5	0/30	0/30	0/30	0/90 = 0%
6.4	2/30	3/30	4/30	9/90 = 10%
8	12/30	5/30	10/30	27/90 = 30%
9.6	20/30	10/30	18/30	48/90 = 53%
15	28/30	26/30	29/30	83/90 = 92%
25	30/30	30/30	30/30	90/90 = 100%

These data show a cut-off concentration of approximately 9-10 mIU/mL.

See Assay cut-off below for more information.

e. Analytical specificity:

Various concentrations of potential cross reactants (hFSH, hLH, and hTSH) were prepared in hCG negative (≤5 mIU/mL) and positive (25 mIU/mL) urine. These test solutions were tested with fifteen replicates of Clearblue

Easy Digital Pregnancy Test from each of three batches of devices.

LH (up to 5000 mIU/mL) and TSH (up to 1.0 mIU/mL) did not interfere with the test. FSH at 1000 mIU/mL and 5000 mIU/mL produced some positive results in the negative samples. However, since 1000 mIU/mL FSH is well above the normal physiological level, this cross-reactivity does not raise any concerns.

Various prescription and over-the-counter drugs and urine metabolites were analyzed for potential interference. The interferents were prepared in hCG negative (≤5 mIU/mL) and positive (25 mIU/mL) urine. These test solutions were tested with five replicates of Clearblue Easy Digital Pregnancy Test from each of three batches of devices.

With the exception of estrone-3-glucoronide (E3G), none of the interferents affected the test results. Initially, one of the five devices gave a negative result for the 25 mIU/mL hCG urine spiked with 1000 ng/mL E3G. The test was repeated, and all five samples gave positive results.

f. Assay cut-off:

In addition to use of spiked urine samples, the cut-off was confirmed using urine samples from early pregnancy. Urine samples from 61 conception cycles of women aged between 18-45 years, with hCG concentrations in the range of 0 to 25 mIU/mL, were used in this study. Each urine sample was assigned to a concentration interval, and the percentage of samples in each concentration interval testing positive was calculated.

All samples with hCG concentrations of 5.0 mIU/mL or below were negative. All samples with hCG concentrations of 20.1 to 24.0 mIU/mL were positive. For samples with hCG concentrations from 5.1 to 20.0 mIU/mL, the percentage of positive results was as follows:

hCG range (mIU/mL)	**% Clearblue Easy Positive**
5.1 to 6.0	6.7%
6.1 to 7.0	25.0%
7.1 to 8.0	20.0%
8.1 to 9.0	37.5%
9.1 to 10.0	50.0%
10.1 to 11.0	50.0%
11.1 to 12.0	0.0%
12.1 to 13.0	77.8%
13.1 to 14.0	100.0%
14.1 to 15.0	91.7%
15.1 to 16.0	100.0%

16.1 to 17.0	100.0%
17.1 to 18.0	100.0%
18.1 to 19.0	83.3%
19.1 to 20.0	85.7%

2. Comparison studies:

a. Method comparison with predicate device:

To determine the accuracy of the Clearblue Easy Digital Pregnancy Test, the subject device was evaluated against a commercially available pregnancy test and quantitative determination of hCG concentration, using urine samples submitted for pregnancy testing. A total of 400 urine samples were tested on three lots of the Clearblue Easy Digital Pregnancy Test and one lot of the commercially available pregnancy test. One sample was excluded from the analysis of results because of a labeling error. The results were as follows:

		Clearblue Easy Digital Pregnancy Test		
Result	Commercial Pregnancy Test	Lot 1	Lot 2	Lot 3
+	100	102	101	102
-	299	297	298	297
Total	399	399	399	399

The results showed five discrepant results between the subject device and commercially available test. The overall agreement was greater than 99%.

For the comparison with the quantitative hCG levels, all samples having hCG concentrations ≤5 mIU/mL were classified as "negative" samples, and all samples having hCG concentrations ≥25 mIU/mL were classified as "positive" samples. Samples with hCG concentration >5 mIU/mL and <25 mIU/mL may result in a positive or a negative result. The results are tabulated below:

				Clearblue Easy Digital Pregnancy Test					
hCG (mIU/mL)	n	Commercial Test		Lot 1		Lot 2		Lot 3	
		+	-	+	-	+	-	+	-
≤5	289	0	289	0	289	1	288	0	289
>5-25	14	6	8	5	9	5	9	4	10
≥25	96	96	0	96	0	96	0	96	0
Total	399	102	297	101	298	102	297	100	299

b. Matrix comparison:

Not applicable

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):

An early pregnancy study using urine samples from 61 conception cycles was conducted. Samples from day -7 to day +2 relative to the first day of the expected period (day 0) were tested with the modified device. A total of 575 samples were tested (35 samples were missing). The results of this study showed 51% (30/59) pregnancy detection 4 days before the first day of the expected period, 82% (49/60) pregnancy detection 3 days before the first day of the expected period, 90% (54/60) pregnancy detection 2 days before the first day of the expected period, and 95% (53/56) pregnancy detection 1 day before the first day of the expected period, using the modified Clearblue Easy Digital Pregnancy Test.

A study was performed to determine the concentration of hCG and the performance of Clearblue Easy Digital Pregnancy Test when tested on urine samples collected from a panel of non-pregnant women of pre-, peri- and post- menopausal age. Samples were collected from 60 non-pregnant women aged 18-40 years (pre-menopausal cohort), 101 non-pregnant women aged 41-55 years (peri-menopausal cohort), and 100 non-pregnant women aged >55 years. The concentration of hCG was determined in each individual urine sample by testing on a quantitative assay. Each sample was also tested on three separate batches of Clearblue Easy Digital Pregnancy Test.

Urine hCG concentrations were as follows:

Cohort	Mean Conc.	Concentration Range
Pre-menopausal	0.06 mIU/mL	0 – 2.3 mIU/mL
Peri-menopausal	1.03 mIU/mL	0 – 16.3 mIU/mL
Post-menopausal	0.82 mIU/mL	0 – 13.2 mIU/mL

Of the 261 samples tested, only four samples had hCG >5 mIU/mL. These four samples were tested for the presence of FSH and P3G and were found to have very high FSH levels, ruling out the possibility of pregnancy. When

tested on the three batches of Clearblue Easy Digital Pregnancy Test, only two samples gave a positive result with one lot. The same samples were negative on the other two lots, as were all the other tests. This represents an incidence of 2/783 (0.3%) false positive results across the study population. Both false positive results were on samples from peri-menopausal women aged ≥50 years.

Studies were performed to evaluate the subject device in the hands of lay users. One hundred and three (103) women aged 18 to 45 years, with varying educational and occupational backgrounds, used the Clearblue Easy Digital Pregnancy Test according to the package insert and provided a sample for professional testing. This included analyzing the sample on a similar, commercially available test as well as determining its hCG concentration. Each consumer also tested a positive (25 mIU/mL) and negative (0 mIU/mL) hCG standard, using the dip procedure.

Most of the consumers used the urine stream procedure. Six volunteer error results and one laboratory error result occurred. For the remaining 96 results, there was 100% agreement between the consumer's result on the new device and the laboratory professional's result on the commercially available test. For the 0 mIU/mL standard, excluding the two protocol deviations, one missing result, and three device errors, there was 100% agreement between the consumer and professional's interpretation of the consumer's result. Although the results from the 25 mIU/mL standard also showed 100% agreement between the consumer and professional's interpretation, there was a higher than expected negative result rate and three device errors. When the Clearblue Easy Digital Pregnancy Test was compared to the quantitative hCG results, 100% of the expected results were obtained, excluding one error result.

In an attempt to reduce the error rate, the instructions were revised by incorporating more prominent instruction about not inverting the device at any time during the test procedure. There was also concern of assembly issue with some of the devices. Therefore, a second consumer study, with an additional 75 women, was conducted. The consumers tested the devices with their own urine stream as well as with the positive (25 mIU/mL) hCG standard, using the dip procedure.

Two out of the 75 urine stream tests performed produced error messages, resulting in a reduced error rate. No error messages occurred with the dip method using the 25 mIU/mL sample, as opposed to the initial study.

One hundred percent (100%) of the consumers felt that the instructions were easy or very easy to understand, and almost 100% felt the results were clear or very clear.

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   The expected values are based on literature studies.

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.