510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K241394

B Applicant

Andon Health Co., Ltd.

C Proprietary and Established Names

iHealth® Early Pregnancy Test; iHealth® Early Pregnancy Test Strip

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LCX	Class II	21 CFR 862.1155 - Human Chorionic Gonadotropin (HCG) Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Human Chorionic Gonadotropin (hCG)

C Type of Test:

Qualitative chromatographic immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The iHealth® Early Pregnancy Test is an OTC in vitro diagnostic test used to assess early pregnancy by detecting the presence of the hCG (human chorionic gonadotropin) hormone in urine. The test device is intended for use as an aid in early detection of pregnancy, in some cases as early as six (6) days before the day of the missed period, i.e., as early as five (5) days before the day of the expected period.

The iHealth® Early Pregnancy Test Strip is an OTC in vitro diagnostic test used to assess early pregnancy by detecting the presence of the hCG (human chorionic gonadotropin) hormone in urine. The test device is intended for use as an aid in early detection of pregnancy, in some cases as early as six (6) days before the day of the missed period, i.e., as early as five (5) days before the day of the expected period.

C Special Conditions for Use Statement(s):

OTC - Over The Counter

D Special Instrument Requirements:

Not applicable

IV Device/System Characteristics:

A Device Description:

The tests are available in two formats: 1) The iHealth Early Pregnancy Test, which consists of a single test strip assembled in a plastic card, with an absorbent tip, designed to be tested in dip or midstream sampling mode; and 2) the iHealth Early Pregnancy Test Strip which consists of a single test strip, designed to be used by dipping the strip into a urine sample collected into the provided collection cup.

B Principle of Operation:

The tests are lateral flow immunoassays for the in vitro detection of human chorionic gonadotropin (hCG) in urine. Testing is conducted by immersing the absorbent tip in urine (dip mode) for 10 seconds or urinating on the absorbent tip (midstream mode) for 2-3 seconds and obtaining the result from the colored lines. After application of the urine specimen, the test result is shown in the result window and read visually after 3-5 minutes of urine application. The hCG present in the urine sample, it is bound by an hCG-2 antibody colloidal gold conjugate present at the front of the test strip forming a complex. This conjugate complex is captured by hCG-1 antibody in the detection zone forming a colored line in the test line region. Concurrently, a line will appear in the quality control zone. If the sample is negative, meaning it lacks hCG or the hCG concentration is below the detection limit, only a line appears in the quality control area. The test result is shown in the result window and read visually 3-5 minutes after urine application. Two distinct colored lines, one line in the control line region and another in the test

line region, indicate a positive test result (pregnant). Absence of a colored line in the test line region and only a colored line in the control line region indicates a negative test result (not pregnant). Absence of a colored line in the control line region, even in the presence of a colored line in the test line region, indicates an invalid test result.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Clearblue ® Early Pregnancy Test

B Predicate 510(k) Number(s):

K213379

C Comparison with Predicate(s):

Device & Predicate Device(s):	K241394	K213379
Device Trade Name	iHealth® Early Pregnancy Test iHealth® Early Pregnancy Test Strip	Clearblue Early Pregnancy Test
General Device Characteristic Similarities		
Intended Use/Indications For Use	Qualitative detection of human hCG for an aid in early detection of pregnancy.	Same
Early Detection Claim	Pregnancy can be detected in some cases as early as six (6) days before the day of the missed period, i.e. as early as five (5) days before the day of the expected period.	Same
hCG Sensitivity	10 mIU/mL	Same
General Device Characteristic Differences		
Time to Result	3-5 minutes	5 minutes
Traceability	World Health Organization (WHO) 5th International Standard (IS) for hCG	World Health Organization (WHO) 4th International Standard (IS) for hCG

VI Standards/Guidance Documents Referenced:

None referenced

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A precision study was performed using negative female urine samples spiked with hCG (traceable to the 5th World Health Organization International Standard (WHO IS)) to obtain samples with hCG concentrations of 0, 3, 5, 7.5, 10, 12.5, 15 and 25 mIU/mL. Each sample was tested using three lots of iHealth® Early Pregnancy Test Strip using dip sampling mode and the iHealth® Early Pregnancy Test using both dip and midstream sampling modes. The tests were performed over the course of five non-consecutive days, at three sites, by nine different operators. A total of 405 replicates were performed per sampling mode per hCG concentration. The results are summarized in the tables below:

iHealth® Early Pregnancy Test Strip (dip sampling mode)

hCG concentration (mIU/mL)	Lot 1		Lot 2		Lot 3		Total result		% Negative	% Positive
	-	+	-	+	-	+	-	+		
0	135	0	135	0	135	0	405	0	0	0
3	135	0	135	0	135	0	405	0	0	0
5	58	77	53	82	59	76	170	235	42.0%	58.0%
7.5	41	94	43	92	35	100	119	286	29.4%	70.6%
10	0	135	0	135	0	135	0	405	0%	100%
12.5	0	135	0	135	0	135	0	405	0%	100%
15	0	135	0	135	0	135	0	405	0%	100%
25	0	135	0	135	0	135	0	405	0%	100%

iHealth® Early Pregnancy Test (dip sampling mode)

hCG concentration (mIU/mL)	Lot 1		Lot 2		Lot 3		Total result		% Negative	% Positive
	-	+	-	+	-	+	-	+		
0	135	0	135	0	135	0	405	0	0	0
3	135	0	135	0	135	0	405	0	0	0
5	62	73	58	77	68	67	188	217	46.4%	53.6%
7.5	48	87	37	98	43	92	128	277	31.6%	68.4%
10	0	135	0	135	0	135	0	405	0%	100%
12.5	0	135	0	135	0	135	0	405	0%	100%
15	0	135	0	135	0	135	0	405	0%	100%
25	0	135	0	135	0	135	0	405	0%	100%

iHealth® Early Pregnancy Test (midstream sampling mode)

hCG concentration (mIU/mL)	Lot 1		Lot 2		Lot 3		Total result		% Negative	% Positive
	-	+	-	+	-	+	-	+		
0	135	0	135	0	135	0	405	0	0	0
3	135	0	135	0	135	0	405	0	0	0
5	67	68	63	72	66	69	196	209	48.4%	51.6%
7.5	44	91	48	87	49	86	141	264	34.8%	65.2%
10	0	135	0	135	0	135	0	405	0%	100%
12.5	0	135	0	135	0	135	0	405	0%	100%
15	0	135	0	135	0	135	0	405	0%	100%
25	0	135	0	135	0	135	0	405	0%	100%

2. Linearity:

Linearity is not applicable since this is a qualitative test.

3. Analytical Specificity/Interference:

Interference from exogenous and endogenous substances

A study was performed to evaluate potential interference from certain exogenous and endogenous substances for the iHealth® Early Pregnancy Test and the iHealth® Early Pregnancy Test Strip devices. Negative, female, human urine samples were used to make samples containing 0 and 10 mIU/mL hCG, which were then spiked with potentially interfering substances at the concentrations listed in the table below. Samples were tested in replicates of five, using three lots of the candidate device. No interference was observed at the concentrations shown in the table below:

Substance	Highest concentration tested that demonstrated no interference
Acetaminophen	20 mg/dL
Acetoacetic Acid	500 mg/dL
Acetylsalicylic Acid	20 mg/dL
Albumin	2000 mg/dL
Ampicillin	20 mg/dL
Ascorbic Acid	20 mg/dL
Atropine	20 mg/dL
Benzoylecgonine	10 mg/dL
B-hydroxybutyrate	1000 mg/dL
Bilirubin	2 mg/dL
Caffeine	20 mg/dL
Cannabinol	10 mg/dL
Codeine	6 µg/dL
EDTA	80 mg/dL
Estriol-17-beta	1400 µg/dL
Ethanol	1.00%

Substance	Highest concentration tested that demonstrated no interference
Gentisic Acid	20 mg/dL
Glucose	2000 mg/dL
Hemoglobin	500 mg/dL
Ketone	20 mg/dL
Methanol	10%
Phenothiazine	20 mg/dL
Phenylpropanolamine	20 mg/dL
Pregnanediol	1500 µg/dL
Salicylic Acid	20 mg/dL
Tetracycline	20 mg/dL
Thiophene	20 mg/dL

Cross-reactivity of structurally-related compounds

A study was performed to evaluate the potential cross-reactivity from luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH) on the iHealth® Early Pregnancy Test and the iHealth® Early Pregnancy Test Strip devices. Negative, female, human urine sample were used to make samples containing 0 and 10 mIU/mL hCG, which were then spiked with the potential cross-reactants: 500 mIU/mL LH, 1000 mIU/mL FSH, and 1 mIU/mL TSH. Samples were tested in replicates of five with each of three lots of the candidate devices. The results demonstrated no cross-reactivity from potential cross-reactants was observed at the tested concentrations.

Effect of urine pH

A study was performed to evaluate the effects of urine pH on the iHealth® Early Pregnancy Test and the iHealth® Early Pregnancy Test Strip devices. Negative, female, human urine sample were used to make samples containing 0 and 10 mIU/mL hCG, which were then adjusted to pH values from 4.0 to 9.0 and tested using the candidate devices. Samples were tested in replicates of five, using three lots of the candidate devices. The results demonstrated that samples within the pH range of 4.0 to 9.0 do not interfere with either positive or negative results from the device.

Effect of urine Specific Gravity

A study was performed to evaluate the effects of urine specific gravity on the iHealth® Early Pregnancy Test and the iHealth® Early Pregnancy Test Strip devices. Negative, female, human urine sample were used to make samples containing 0 and 10 mIU/mL hCG, which were then adjusted to specific gravity values from 1.000 to 1.035 and tested using the candidate devices. Samples were tested in replicates of five, using three lots of the candidate device. The results demonstrated that samples within the specific gravity range of 1.000 to 1.035 do not interfere with either positive or negative results from the device.

Effect of hCG β-core (hCGβcf) fragment

A study was performed to evaluate the effects hCGβcf on the iHealth® Early Pregnancy Test and the iHealth® Early Pregnancy Test Strip devices. Negative, female, human urine samples and were used to make samples containing 0 and 10 mIU/mL hCG, which were then spiked with hCG β-core fragment concentrations of 250,000 pmol/L, 500,000 pmol/L, and 1,000,000 pmol/L. Samples were tested in replicates of five, using three lots of the candidate

devices. The results show that the performance of the candidate device is not affected by concentrations of hCGβcf up to 1,000,000 pmol/L.

High dose hook effect study
A study was performed to evaluate the high dose hook effect on the iHealth® Early Pregnancy Test and the iHealth® Early Pregnancy Test Strip devices. Negative, female, human urine samples were spiked up to 1,000,000 mIU/mL hCG and tested using the candidate device. Samples were tested in replicates of five, using three lots of the candidate device. No hook effect was observed at concentrations of up to 1,000,000 mIU/mL hCG.

4. Assay Reportable Range:

   Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The tests are calibrated against the World Health Organization (WHO) International Standard (IS) 5th Edition, NIBSC code 07/364.

6. Detection Limit:
   The detection limit was determined in the precision study (see Section VII.A.1. above).

7. Assay Cut-Off:

   The device cutoff is 10 mIU/mL hCG. See Precision/Reproducibility (Section VII.A.1.) sections above.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   A total of 204 urine samples were collected from women whose ages ranged from 18 to 45 years, who suspect they are in the early stages of pregnancy. Approximately half of the women were suspected to be pregnant and most of them were in the early stage of pregnancy (less than 5 weeks). The samples were masked and randomized prior to testing by professionals using the candidate device (iHealth® Early Pregnancy Test in dip mode and midstream mode and iHealth® Early Pregnancy Test Strip in dip mode) and the predicate device (Clearblue Early Pregnancy Test in dip mode). One hundred and three (103) samples were tested using the iHealth® Early Pregnancy Test Strip and 101 samples were tested using the iHealth® Early Pregnancy Test Stick. Summary results are presented in the tables below.

   iHealth® Early Pregnancy Test Strip (dip mode)

Candidate Device		Predicate device		Total
		Positive	Negative	
iHealth® Early Pregnancy Test Strip	Positive	54	0	54
	Negative	0	49	49
	Total	54	49	103

iHealth® Early Pregnancy Test Stick (dip and midstream mode)

Candidate Device		Predicate device		Total
		Positive	Negative	
iHealth® Early Pregnancy Test Strip	Positive	55	0	55
	Negative	0	46	46
	Total	55	46	101

The sponsor also provided a study of 502 women which additionally supported the accuracy of the device.

2. Matrix Comparison:

Not applicable. The device is intended for urine samples only.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Detection of hCG in Early Pregnancy Clinical Samples:

A total of 830 urine samples from days +1 to -8 relative to the day of the expected menstrual period (EMP) were collected from women aged 18 to 55 years from the intended use population. Each sample was tested using both the iHealth® Early Pregnancy Test Strip (dip mode) and the iHealth® Early Pregnancy Test (dip mode and midstream modes) across three lots of each device format (stick and strip). The early pregnancy detection results are summarized in table below.

Day relative to EMP	Sample (n) per sampling mode	iHealth® Early Pregnancy Test Strip (dip mode)		iHealth® Early Pregnancy Test (dip mode)		iHealth® Early Pregnancy Test (midstream mode)	
		Pregnant (n)	Pregnant (%)	Pregnant (n)	Pregnant (%)	Pregnant (n)	Pregnant (%)
-8	83	4	5	4	5	5	6
-7	83	11	13	10	12	11	13
-6	83	23	28	22	27	22	27
-5	83	65	78	65	78	65	78
-4	83	77	93	77	93	77	93
-3	83	82	99	82	99	82	99

Day relative to EMP	Sample (n) per sampling mode	iHealth® Early Pregnancy Test Strip (dip mode)		iHealth® Early Pregnancy Test (dip mode)		iHealth® Early Pregnancy Test (midstream mode)	
		Pregnant (n)	Pregnant (%)	Pregnant (n)	Pregnant (%)	Pregnant (n)	Pregnant (%)
-2	83	82	99	82	99	82	99
-1	83	83	100	83	100	83	100
0	83	83	100	83	100	83	100
+1	83	83	100	83	100	83	100

Lay user study

A lay user study was conducted with 204 volunteers with diverse educational and occupational backgrounds who were between the age of 18 and 45. This included 103 lay users using the iHealth® Early Pregnancy Test Strip and 101 lay users using the iHealth® Early Pregnancy Test. Lay users tested their own urine specimen. Each lay user also provided a sample for professional testing. Then the results of lay-user tests were compared to results reported by a laboratory professional. The data shows that the agreement between lay-user results and professional results was 100% (below):

iHealth® Early Pregnancy Test Strip (dip mode)

Lay user	Professional		
	Pregnant	Not Pregnant	Total
Positive	54	0	54
Negative	0	49	49
Total	54	49	103

iHealth® Early Pregnancy Test (dip and midstream mode)

Lay user	Professional		
	Pregnant	Not Pregnant	Total
Positive	55	0	55
Negative	0	46	46
Total	55	46	101

The sponsor also provided a study of 369 women which additionally supported the accuracy of the device.

Lay user spiked sample study

A second lay user study was conducted with a total of 100 women with diverse educational and professional backgrounds between the ages of 18 years to 55. Lay users performed the testing using samples spiked with 0, 2, 3, 5, 10 and 15 mIU/mL hCG using one lot each of the iHealth® Early Pregnancy Test Strip using dip mode and the iHealth® Early Pregnancy Test using both dip and simulated midstream modes. Results are summarized below.

hCG level (mIU/mL)	iHealth® Early Pregnancy Test Strip (dip mode)	iHealth® Early Pregnancy Test (dip mode)	iHealth® Early Pregnancy Test (simulated midstream mode)
	% Positive	% Positive	% Positive
0	0%	0%	0%
2	0%	0%	0%
3	0%	0%	0%
5	46%	43%	44%
10	100%	100%	100%
15	100%	100%	100%

Specificity Study to Determine False Positive Result Rate

A study was performed to determine the incidence of false positive test results from iHealth® Early Pregnancy Test and iHealth® Early Pregnancy Test Strip. Urine samples were collected from 300 women from each of three cohorts: non-pregnant pre-menopausal women aged 18-40 years, non-pregnant peri-menopausal women aged 41-55 years, and non-pregnant post-menopausal women > 55 years of age. Samples were tested by trained technicians with three lots of the candidate device using both the iHealth® Early Pregnancy Test (dip mode) and the iHealth® Early Pregnancy Test Stick (dip mode and midstream mode). No false positive results were observed for any of the age groups. Results of the study are shown in the table below:

Summary of Specificity Testing

Format	Cohort	# of Samples	Positive Results (%)
iHealth® Early Pregnancy Test Strip (dip mode)	Non-pregnant, pre-menopausal	100	0/100 (0%)
	Non-pregnant, peri-menopausal	100	0/100 (0%)
	Non-pregnant, post-menopausal	100	0/100 (0%)
	All non-Pregnant	300	0/100 (0%)
iHealth® Early Pregnancy Test Stick (dip mode)	Non-pregnant, pre-menopausal	100	0/100 (0%)
	Non-pregnant, peri-menopausal	100	0/100 (0%)
	Non-pregnant, post-menopausal	100	0/100 (0%)
	All non-Pregnant	300	0/100 (0%)
iHealth® Early Pregnancy Test Stick (midstream mode)	Non-pregnant, pre-menopausal	100	0/100 (0%)
	Non-pregnant, peri-menopausal	100	0/100 (0%)
	Non-pregnant, post-menopausal	100	0/100 (0%)
	All non-Pregnant	300	0/100 (0%)

A Clinical Cut-Off:

Not applicable

B Expected Values/Reference Range:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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