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

A. 510(k) Number:

k112870

B. Purpose for Submission:

New device

C. Measurand:

Human chorionic gonadotropin (hCG)

D. Type of Test:

Qualitative, Immunochromatographic

E. Applicant:

SPD Swiss Precision Diagnostics GMBH

F. Proprietary and Established Names:

Clearblue Advanced Pregnancy Test with Weeks Estimator

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LCX	Class II	21 CFR§ 862.1155	Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for Use below.

2. Indication(s) for use:

The Clearblue Advanced Pregnancy Test with Weeks Estimator is an over-the-counter urine hCG test which is intended for the detection of pregnancy. The test detects hCG in some cases from four days before the expected period (which is 5 days before the day of the missed period).

This test is only intended for individual use at home. It is not intended for use in a healthcare setting.

This test contains a "Weeks Estimator." The "Weeks Estimator" is meant solely as an estimate for the consumer and is not intended as a substitute for a doctor's clinical diagnosis. The 'Weeks Estimator' is not intended for multiple pregnancies. The estimate provided by the device may be inaccurate in these cases.

This test cannot be used to determine the duration of pregnancy or to monitor the progression of pregnancy. Your doctor determines how many weeks pregnant you are based on the first day of your last menstrual period and ultrasound results. This test provides a different estimate that cannot be substituted for a doctor's determination of gestational age. Only your doctor can provide a reliable estimate of gestational age and only your doctor can monitor pregnancy progression. You should seek qualified prenatal care if you suspect you are pregnant.

3. Special conditions for use statement(s):

For in vitro diagnostic use

For over-the-counter use

The following limitations must appear in the device's labeling:

1. Box Labeling:
   a) Performance of the Weeks Estimator should not be displayed on the box labeling. Box labeling should instruct users to see the package insert for test instructions and for more information on the Weeks Estimator.
   b) The terms "*Accurate* or *Accuracy*" should not be used on the box labeling.

2. Package Insert:
   a) Weeks Estimator results should not be expressed as "weeks pregnant" and should only be explained as the number of weeks that may have passed since ovulation.
   b) Weeks Estimator performance should only be presented as follows:

Result	Pregnant 1-2	Pregnant 2-3	Pregnant 3+
What does this mean?	Your result is Pregnant and you may be 1-2 weeks since ovulation	Your result is Pregnant and you may be 2 and up to 3 weeks since ovulation	Your result is Pregnant and you may be more than 3 weeks since ovulation
How your doctor may date your pregnancy (weeks pregnant)	3-4 weeks	4-5 weeks	5+ weeks

- The Weeks Estimator result is determined by the level of hCG in your urine. The level of hCG varies from woman to woman and therefore the Weeks Estimator may give misleading results. All results should be confirmed by your doctor, especially when making decisions about future medical care. Only your doctor can determine whether your pregnancy is healthy.

- Your doctor determines how many weeks pregnant you are based on the first day of your last menstrual period and ultrasound results. This test provides a different estimate. Please note that the doctor may date your pregnancy differently from the information shown in this table, since pregnancy dating is dependent on the circumstances of the patient.

- Agreement of Weeks Estimator results with clinical findings ranged widely from 45-99%.

3. The Indications for Use Statement must be prominently displayed in all labeling, including pouch box, and carton labels, and instructions for use, in close proximity to the trade name, of a similar point size, and in bold and shall be conveyed accurately – including any limitations – in all promotional materials.

4. Special instrument requirements:

   None required

I. Device Description:

The Clearblue Advanced Pregnancy Test with Weeks Estimator is a ready-to-use device that consists of a plastic stick, which contains an absorbent tip that protrudes from the end of the device. The test is performed by placing the absorbent tip of the device downward in the urine stream for 5 seconds or by immersing the absorbent tip

into a container of urine for 20 seconds.

The detection of hCG in the urine sample above a threshold is indicated by the "Pregnant" result on the display and "Weeks Estimator" result (PREGNANT 1-2, PREGNANT 2-3, or PREGNANT 3+). These three pregnant categories estimate the number of weeks since ovulation. The test uses a semi-quantitative measurement of hCG concentration in urine to categorize each positive result into one of the three pregnancy categories. If the concentration of hCG in the sample is below the minimum detection threshold the display will show a "Not Pregnant" result.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Clearblue Easy Digital Pregnancy Test

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

   K060128

3. Comparison with predicate:

Item	Candidate Device	Predicate Device
Intended Use	Clearblue Advanced Pregnancy Test with Weeks Estimator device is intended for the semi-quantitative detection of human chorionic gonadotropin (hCG) in urine to help in the early determination of pregnancy	Same
Weeks Estimator Feature	Pregnant 1-2, Pregnant 2-3, or Pregnant 3+	No weeks estimator feature
Earliest day of use	4 days before expected period	Same
Specimen type	Urine	Same
Principle	Lateral flow immunochromatographic sandwich assay	Same
Test Format	Test Strip/Dip-Cup	Same
Sampling time	5 seconds in urine stream 20 seconds in cup	Same

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

None were referenced

L. Test Principle:

The test is a sandwich immunoassay employing monoclonal antibodies specific for hCG and uses chromatographic principles to separate bound and free colored label. The device contains two test chips – a high sensitivity chip and a low sensitivity chip that each contains a nitrocellulose solid phase, an antibody-latex conjugate mobile phase, and a test zone containing immobilized monoclonal antibody specific for hCG. The low sensitivity chip also contains a control zone containing immobile monoclonal goat anti-rabbit IgG. The device reader measures the reflectance of light incident on the test and control lines and flow along the test chips to determine the test result or if an error has occurred.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   A combined precision/sensitivity study was performed where the candidate device was challenged over 3 days, with 6 different operators who conducted tests on 3 lots of devices. Twenty-eight urine standards were used in the study in a range from 0 mIU/mL to 4621 mIU/mL hCG. The range of standards tested incorporated a negative control, and hCG concentrations at the "Pregnant 1-2" cut-off threshold (10 mIU/mL), "Pregnant 2-3" cut-off threshold (156 mIU/mL), "Pregnant 3+" cut-off threshold (2600 mIU/mL), and concentrations ± 20-80% of the thresholds. Only 3 operators conducted testing on any one standard. Percentage results representative of data from all three tested lots are provided below. Results were similar for each tested lot.

	Actual hCG Conc. mIU/ml	Lot Results			
		(-)	1-2	2-3	3+
Negative – Control	0.06	90/90	0/90	0/90	0/90
-80% of Pregnant 1-2 threshold	2.0	90/90	0/90	0/90	0/90
-60% of Pregnant 1-2 threshold	4.0	90/90	0/90	0/90	0/90
-40% of Pregnant 1-2 threshold	6.2	100/100	0/100	0/100	0/100
-20% of Pregnant 1-2 threshold	8.3	90/90	0/90	0/90	0/90
Pregnant 1-2 threshold	10.2	55/90	35/90	0/90	0/90
+20% of Pregnant 1-2 threshold	12.0	28/90	62/90	0/90	0/90
+40% of Pregnant 1-2 threshold	14.1	2/90	88/90	0/90	0/90
+60% of Pregnant 1-2 threshold	15.7	1/90	89/90	0/90	0/90
+80% of Pregnant 1-2 threshold	17.7	0/90	90/90	0/90	0/90
-80% of Pregnant 2-3 threshold	30.9	0/90	90/90	0/90	0/90
-60% of Pregnant 2-3 threshold	61.5	0/90	90/90	0/90	0/90
-40% of Pregnant 2-3 threshold	93.2	0/90	90/90	0/90	0/90
-20% Pregnant 2-3 threshold	121	0/90	89/90	1/90	0/90
Pregnant 2-3 threshold	153	0/90	71/90	19/90	0/90
+20% of Pregnant 2-3 threshold	184	0/90	33/90	57/90	0/90
+40% of Pregnant 2-3 threshold	214	0/90	18/90	72/90	0/90
+60% of Pregnant 2-3 threshold	250	0/90	3/90	87/90	0/90

	Actual hCG Conc. mIU/ml	Lot Results			
		(-)	1-2	2-3	3+
+80% of Pregnant 2-3 threshold	276	0/90	3/90	87/90	0/90
-80% of Pregnant 3+ threshold	504	0/90	0/90	90/90	0/90
-60% of Pregnant 3+ threshold	1021	0/90	0/90	90/90	0/90
-40% of Pregnant 3+ threshold	1599	0/90	0/90	90/90	0/90
-20% of Pregnant 3+ threshold	2103	0/90	0/90	88/90	2/90
Pregnant 3+ threshold	2518	0/90	0/90	69/90	21/90
+20% of Pregnant 3+ threshold	3229	0/90	0/90	25/90	65/90
+40% of Pregnant 3+ threshold	3618	0/90	0/90	5/90	85/90
+60% of Pregnant 3+ threshold	4176	0/90	0/90	0/90	90/90
80% of Pregnant 3+ threshold	4621	0/90	0/90	0/90	90/90

b. Linearity/assay reportable range:

Not applicable

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

The device is standardized to the World Health Organization's 4th International Standard for Chorionic Gonadotropin.

d. Detection limit:

Sensitivity/cut-off studies were combined with the precision study. See results in Section 1.a. above. The following are the cut-off thresholds of the candidate device:

- Not pregnant/pregnant 1-2 threshold = 10 mIU/mL
- Pregnant 1-2/pregnant 2-3 threshold = 156 mIU/mL,

- Pregnant 2-3/pregnant 3+ threshold = 2600 mIU/mL.

e. Analytical specificity:

Potential cross-reactants, endogenous, and exogenous interferents listed in the table below were tested on three batches of the candidate device. These substances were prepared at the indicated test levels displayed in the table below using urine from non-pregnant women. Urine samples used for test sample preparation were also spiked to obtain the following concentrations of hCG: < 5 mIU/mL (negative), 25 mIU/mL (representative of Pregnant 1-2), 250 mIU/mL (representative of Pregnant 2-3), and 5000 mIU/mL (representative of Pregnant 3+). Each test sample was analyzed 30 times per device batch.

Substance	Low Test Level (Normal)	High Test Level
Cross Reactants		
TSH	N/A	1 mIU/mL
LH	N/A	1000 mIU/mL
FSH	N/A	1000 mIU/mL
Endogenous		
Albumin	0.2 mg/mL	3.0 mg/mL
Estrone ß-D gluconide	62 ng/mL	620 ng/mL
Glucose	1 mg/mL	10 mg/mL
Hemoglobin	10 µg/mL	100 µg/mL
5ß - Pregnane-3ά, 20ά-diol glucuronide	4 µg/mL	40 µg/mL
Urea	30 mg/mL	N/A
Uric Acid	750 mg/mL	N/A
Urobilinogen	10 µg/mL	100 µg/mL
Exogenous		
Acetylsalicylic Acid	0.36 mg/mL	1.0 mg/mL
Ascorbic Acid	30 µg/mL	150 µg/mL
Caffeine	0.12 mg/mL	1.2 mg/mL
Clomiphene Citrate	8 µg/mL	24 µg/mL
Cotinine	2 µg/mL	40 µg/mL
Ethanol	0.1% v/v	1% v/v
Ibuprofen	36 µg/mL	100 µg/mL
Oxytetracycline	300 µg/mL	N/A
Paracetamol	200 µg/mL	600 µg/mL
Tetracycline	300 µg/mL	N/A

f. Assay cut-off:

Sensitivity/cut-off studies were combined with the precision study. See results in Section 1.a. above for samples with hCG concentration in the range of 0 to 4621 mIU/mL hCG. Additional results for spiked samples with hCG concentrations ≤ 25 mIU/mL are provided in the table below.

	Percentage Results					
	Batch 1		Batch 2		Batch 3	
hCG (mIU/mL)	Not Pregnant	Pregnant 1-2	Not Pregnant	Pregnant 1-2	Not Pregnant	Pregnant 1-2
0.06	100.0	0.0	100.0	0.0	100.0	0.0
2	100.0	0.0	100.0	0.0	100.0	0.0
4	100.0	0.0	100.0	0.0	100.0	0.0
5.3	100.0	0.0	100.0	0.0	100.0	0.0
6.2	100.0	0.0	100.0	0.0	98.9	1.1
8.3	100.0	0.0	96.6	3.4	96.7	3.3
10.2	61.1	38.9	55.6	44.4	56.7	43.3
12	31.1	68.9	20.0	80.0	12.2	87.8
14.1	2.2	97.8	2.2	97.8	2.2	97.8
15.7	1.1	98.9	1.1	98.9	1.1	98.9
17.7	0.0	100.0	0.0	100.0	0.0	100.0
20.1	0.0	100.0	0.0	100.0	0.0	100.0
25	0.0	100.0	0.0	100.0	0.0	100.0

The cut-off concentration for a pregnant/not pregnant result was concluded to be approximately 10 mIU/mL hCG.

2. Comparison studies:

a. Method comparison with predicate device:

Three hundred female urine samples were analyzed by two trained laboratory technicians using the candidate device (ClearBlue Advanced) and the commercially available predicate device (ClearBlue Digital). The samples were evaluated using 3 batches of the candidate device. The results per batch are summarized as follows:

Batch 1		ClearBlue Digital		Subtotal
ClearBlue Advance		+	-	
	+	112	0	112
	-	0	188	188
Subtotal		112	188	300

Batch 2		ClearBlue Digital		Subtotal
ClearBlue Advance		+	-	
	+	112	1	113
	-	0	187	187
Subtotal		112	188	300

Batch 3		ClearBlue Digital		Subtotal
ClearBlue Advance		+	-	
	+	112	3	115
	-	0	185	185
Subtotal		112	188	300

Note: The predicate does not have a weeks estimator feature, so only pregnant or not pregnant results were evaluated for method comparison. For batch 2, the one discrepant sample contained a hCG concentration of 6.1 mIU/mL. For batch 3, two of the discrepant samples were erroneously categorized on the predicate as negative, but actually contained hCG concentrations of 20.6 mIUmL and 14.5 mIU/mL. The other discrepant sample in batch 3 contained a hCG concentration of 6.1 mIU/mL (1 sample).

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):

A dip method lay-user study was conducted using 200 female subjects up to 45 years of age. Upon arrival, subjects were provided a test kit package containing the following: instructions for use, pre- and post- testing

questionnaires on the instructions for use, randomized standards, and the candidate device. The subjects were told to perform the tests according to the package insert. Trained laboratory technicians also tested the urine samples on the candidate device. Thirteen total standards (including a negative control) with hCG concentrations from 0.06 to 6125 mIU/mL (representative of each of the .three device thresholds and concentrations ± 20% of each threshold), were used in the study. Lay-users and technicians only evaluated 7 standards each. Post-testing questionnaires were administered after testing the first standard. The results of the comparison between lay users and trained technicians on obtaining a pregnant/not pregnant result with the candidate device are as follows:

Target Concentration	hCG mIU/ml				
		Lay-User		Technician	
		(-)	(+)	(-)	(+)
Negative	0.06	200/200	0/200	200/200	0/200
-20% of Pregnant 1-2 threshold	8.3	97/100	3/100	93/100	7/100
Pregnant 1-2 threshold	10.2	47/100	53/100	59/100	41/100
+20% of Pregnant 1-2 threshold	12.0	34/100	66/100	22/100	78/100
Consistently in Pregnant 1-2 category	30.9	0/100	100/100	0/100	100/100
-20% of Pregnant 2-3 threshold	121	0/100	100/100	0/100	100/100
Pregnant 2-3 threshold	153	0/99	99/99	0/99	99/99
+20% of Pregnant 2-3 threshold	184	0/100	100/100	0/100	100/100
Consistently in Pregnant 2-3 category	799	0/99	99/99	0/99	99/99

Target Concentration	hCG mIU/ml				
		Lay-User		Technician	
		(-)	(+)	(-)	(+)
-20% of Pregnant 3+ threshold	2103	0/100	100/100	0/100	100/100
Pregnant 3+ threshold	2518	0/100	100/100	0/100	100/100
+20% of Pregnant 3+ threshold	3229	0/100	100/100	0/100	100/100
Consistently in Pregnant 3+ category	6125	0/100	100/100	0/100	100/100

An additional lay-user study was also conducted with the candidate device to evaluate the in-stream testing method, using 133 female subjects aged 18-45 years. Lay-users were asked to collect the same urine void sample in a container so that trained laboratory technicians could also test the urine samples on the candidate device. Of the 133 samples evaluated, 8 samples either produced an error result or the dip-method (rather than the in-stream method) was erroneously used for testing. A total of 124 samples were tested appropriately and without error. Results from these 124 samples are shown in the table below.

	Lab Technicians			Subtotal
Lay Users		+	-	
	+	94	0	94
	-	0	30	30
Subtotal		94	30	124

The package insert survey results collected showed that most of the women in the lay-user studies had at least some high school education. All volunteers understood how to use the device (in-stream and dip methods) and 92.5% of volunteers understood the importance of holding the device in the correct orientation to obtain accurate results. Volunteers understood the implications of the results from the device, with 100% of volunteers answering they should see a doctor if the test result is positive (pregnant), 94% responding they should test again when their menstrual cycle is due if tested early, and 92.5% answering they should test again in 3 days time if their menstrual cycle is overdue. Volunteers also understood that accuracy of the "Weeks Estimator" varied within each of the estimator categories (87.2 to 93.2%) and that there is

a difference between the way a doctor would date a pregnancy and the "Weeks Estimator" result (89.5 to 90.2%).

An early pregnancy study was conducted using 100 urine samples collected from non-pregnant women expecting to become pregnant. These samples were collected on days -6 to 1+ relative to the day of expected period. Each sample was tested on three separate lots of the candidate device and results were recorded. Results were as follows:

Day in Cycle Relative to Expected Period	Overall Pregnancy Detection Rate (%)	Pregnancy Detection Rate Range seen across batches (%)
-6 days	4.1	0.0 - 9.8
-5 days	26.1	16.2 - 38.5
-4 days	65.5	50.0 - 83.3
-3 days	90.6	81.6 - 97.4
-2 days	97.9	94.7 - 100
-1 day	98.8	93.9 - 100
-0 days	99.0	97.1 - 100
+1 day	99.1	97.3 - 100

A study was performed to evaluate the performance of the candidate device when tested on urine samples collected from a panel of non-pregnant women of pre-, peri-, and post- menopausal age. Samples were collected from 100 non pregnant women aged 18-40 years (pre-menopausal), 101 non-pregnant women aged 41-55 years (peri-menopausal), and 100 non-pregnant women aged > 55 years (menopausal). 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 the candidate device. All samples tested negative (not pregnant).

A clinical study was conducted to evaluate performance of the "Weeks Estimator" feature of the device compared to clinical truth (gestational age). A total of 153 volunteer samples, representative of single viable pregnancies were included in the study. Agreement of "Weeks Estimator" results from this study with clinical findings ranged widely from 45-99%. Limitations are included in the labeling of the device to inform consumers of Week Estimator performance and to inform consumers that the "Weeks Estimator" is meant solely as an estimate. See Special Conditions for Use Statements in section H. of this decision summary.

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Not applicable

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.