August 13, 2021

SPD Swiss Precision Diagnostics GmbH
% Kamila Przedmojska
Senior Regulatory Affairs Specialist
SPD Development Company Limited
Priory Business Park
Bedford MK44 3UP
United Kingdom

Re: K200913
Trade/Device Name: Clearblue® Early Digital Pregnancy Test
Regulation Number: 21 CFR 862.1155
Regulation Name: Human Chorionic Gonadotropin (HCG) Test System
Regulatory Class: Class II
Product Code: LCX
Dated: November 4, 2020
Received: November 6, 2020

Dear Kamila Przedmojska:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k200913

Device Name
Clearblue® Early Digital Pregnancy Test

Indications for Use *(Describe)*
The Clearblue® Early Digital Pregnancy Test is an over-the-counter chromatographic immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine. This digital test 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 test is intended for home use.

Type of Use *(Select one or both, as applicable)*

☐ Prescription Use (Part 21 CFR 801 Subpart D) ☒ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

A. Submitted By:

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B. Contact Person:

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C. Date Prepared: 11 August, 2021

D. Device Name: Clearblue® Early Digital Pregnancy Test

Product Code:	LCX
Common name:	Kit, Test, Pregnancy, hCG, over the counter
Classification:	Class II
Product code:	LCX
Regulation Description:	Human chorionic gonadotropin (hCG) test system
Regulation number:	21CFR 862.1155

E. Predicate Device: k123567, FIRST RESPONSE™ Gold Digital Pregnancy Test (k123567)

F. Indication for Use

The Clearblue® Early Digital Pregnancy Test is an over-the-counter chromatographic immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine. This digital test 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 test is intended for home use.

G. Device Description

The Clearblue® Early Digital Pregnancy Test is an over-the-counter (OTC), digital pregnancy test with sensitivity to 10mIU/ml hCG (hormone human chorionic gonadotrophin) and is indicated for use up to 6 days before the missed period (5 days before expected period). The device employs an immunochromatographic sandwich assay to detect hCG on a lateral flow test strip. The result is displayed to the user, in words, on an LCD.

H. Substantial Equivalence Information

Predicate device name:
FIRST RESPONSE™ Gold Digital Pregnancy Test

Predicate (k) number:
k123567

Comparison with predicate:

Table 1 Similarities and differences between Clearblue® Early Detection Pregnancy Test and the predicate FIRST RESPONSE™ Early Results Pregnancy Test

Component	**Clearblue® Early Digital Pregnancy (Proposed Device)**	**FIRST RESPONSE™ Gold Digital Pregnancy Test (Predicate Device)**
Similarities		
Intended Use	Qualitative detection of human hCG for an aid in early detection of pregnancy	Same

Component	Clearblue® Early Digital Pregnancy (Proposed Device)	FIRST RESPONSE™ Gold Digital Pregnancy Test (Predicate Device)
Target User	Over-The-Counter use	Same
Device format	Single Use	Same
Sample Matrix	Urine	Same
Analyte	hCG	Same
hCG Sensitivity	10mIU/ml	Same
Traceability	WHO 4th International Standard for hCG	Same
Test Principle	Lateral flow qualitative chromatographic immunoassay with digital result display	Same
Electronic components	Microprocessor with specific circuitry and algorithm. LCD readout with battery as power source.	Same
Sample application	In-stream and dip methods	Same
Early Claim	Pregnancy can be detected as early as six days before the date of the missed period (five days before expected period).	Same
Differences		
hCG Isoforms Detected	Intact hCG	Intact hCG Hyperglycosylated hCG hCG β-subunit hCG β-core fragment
Sampling time	The user is instructed to remove the absorbent tip from the urine when the Stop Light begins to flash (usually 5 seconds for both sampling methods)	5 seconds for both sampling methods

Component	Clearblue® Early Digital Pregnancy (Proposed Device)	FIRST RESPONSE™ Gold Digital Pregnancy Test (Predicate Device)
Time to results	1 -5 minutes	3 minutes
Result Display	Pregnant / Not Pregnant displayed in words	YES+ (for Pregnant results) NO- (for Not Pregnant result)

I. Test Principle

The Clearblue® Early Digital Pregnancy test is a lateral flow sandwich immunoassay employing monoclonal antibodies that are specifically directed against the alpha and beta sub-units of hCG.

To use the test, the user either urinates directly onto the absorbent wick or collects a sample in a container and dips the absorbent wick into the collected sample until the Stop Light begins to flash (which usually takes 5 seconds for both sampling methods). Once the device self-calibration process is completed, a progress bar symbol appears on the display, indicating that test is working and counting down the time to result. The test is complete after a result (Pregnant/ Not Pregnant in words) or an error (book symbol) is displayed on the LCD. This occurs within 1-5 minutes of sample detection.

J. Performance characteristics

1. Analytical Performance

a) Precision/Reproducibility

A pooled negative urine was spiked with hCG to provide nine urine standards with the hCG concentrations of 0, 3, 4.5, 6, 7.5, 9, 10, 12.5 and 25 mIU/ml. The nine standards were each tested with devices from three different batches using both dip and simulated in-stream sampling methods.

The study was performed by three technicians over three non-consecutive days. On each test day, 3 technicians tested 5 devices each per batch, per standards, per sampling method.

The results demonstrate that the analytical sensitivity of the Clearblue® Early Digital Pregnancy Test device is 10mIU/ml. The analytical cut-off

value (approximately half of the devices yield positive results and the remainder yield negative) has been determined as 7.6 mIU/ml.

The results are summarised in the tables below:

Overall Precision Results of Clearblue® Early Digital Pregnancy Test

hCG Standard (mIU/ ml)	Total Samples (n)	Clearblue® Early Digital Pregnancy Test Overall Results						Total Pregnant (%)
		Dip method			Simulated in stream method			
		Not Pregnant (n)	Pregnant (n)	Pregnant Results (%)	Not Pregnant (n)	Pregnant (n)	Pregnant Results (%)	
0	324	162	0	0.0	162	0	0.0	0.0
3	324	162	0	0.0	162	0	0.0	0.0
4.5	324	159	3	1.9	155	7	4.3	3.1
6	324	147	15	9.3	141	21	13.0	11.1
7.5	324	106	56	34.6	88	74	45.7	40.1
9	324	21	141	87.0	15	147	90.7	88.9
10	324	0	162	100.0	0	162	100.0	100.0
12.5	324	0	162	100.0	0	162	100.0	100.0
25	324	0	162	100.0	0	162	100.0	100.0

Percentage Pregnant Results for Each hCG Standard by Technician

hCG Standard (mIU/ ml)	Technician 1		Technician 2		Technician 3	
	P/NP* (n)	Pregnant Results (%)	P/NP* (n)	Pregnant Results (%)	P/NP* (n)	Pregnant Results (%)
0	0/108	0.0	0/108	0.0	0/108	0.0
3	0/108	0.0	0/108	0.0	0/108	0.0
4.5	1/107	0.9	5/103	4.6	4/104	3.7
6	11/97	10.2	12/96	11.1	13/95	12.0
7.5	37/71	34.3	49/59	45.4	44/64	40.7
9	97/11	89.8	95/13	88.0	96/12	88.9
10	108/0	100.0	108/0	100.0	108/0	100.0
12.5	108/0	100.0	108/0	100.0	108/0	100.0
25	108/0	100.0	108/0	100.0	108/0	100.0

*Pregnant/Not Pregnant Results

Percentage Pregnant Results for each hCG standard by Day

Hcg Standard (Miu/ ml)	Day 1		Day 2		Day 3	
	P/NP* (n)	Pregnant Results (%)	P/NP* (n)	Pregnant Results (%)	P/NP* (n)	Pregnant Results (%)
0	0/108	0.0	0/108	0.0	0/108	0.0
3	0/108	0.0	0/108	0.0	0/108	0.0
4.5	2/106	1.9	3/105	2.8	5/103	4.6
6	14/94	13.0	7/101	6.5	15/93	13.9
7.5	37/71	34.3	45/63	41.7	48/60	44.4
9	96/12	88.9	95/13	88.0	97/11	89.8
10	108/0	100.0	108/0	100.0	108/0	100.0
12.5	108/0	100.0	108/0	100.0	108/0	100.0
25	108/0	100.0	108/0	100.0	108/0	100.0

*Pregnant/Not Pregnant Results

Table 4 Percentage Pregnant Results for each hCG standard by Batch

hCG Standard (mIU/ ml)	NEN0008/1R		NEN0008/2R		NEN0008/3	
	P/NP* (n)	Pregnant Results (%)	P/NP* (n)	Pregnant Results (%)	P/NP* (n)	Pregnant Results (%)
0	0/108	0.0	0/108	0.0	0/108	0.0
3	0/108	0.0	0/108	0.0	0/108	0.0
4.5	3/105	2.8	5/103	4.6	2/106	1.9
6	15/93	13.9	11/97	10.2	10/98	9.3
7.5	53/55	49.1	38/70	35.2	39/69	36.1
9	97/11	89.8	98/10	90.7	93/15	86.1
10	108/0	100.0	108/0	100.0	108/0	100.0
12.5	108/0	100.0	108/0	100.0	108/0	100.0
25	108/0	100.0	108/0	100.0	108/0	100.0

*Pregnant/Not Pregnant Results

b) Linearity/assay reportable range:

Not applicable. This is a qualitative device.

c) High dose hook effect study:

Negative pooled urine was spiked with hCG to concentrations of <0.5, 10 and 1,000,000mIU/ml and tested with 5 replicates per each of three batches. No hook effect was observed at tested concentration.

d) Traceability

The tests are calibrated against the WHO 4th International Standards for Chorionic Gonadotropin (hCG).

e) Stability

The claimed shelf life of the device stored in the sealed foil pouches at room temperature is 39 months.

f) Detection Limit (Sensitivity)

See Precision/Reproducibility section.

g) Analytical Specificity

Structure not-related compounds

Interfering substances
The Clearblue® Early Detection Pregnancy Test devices were tested with potentially interfering substances. Each interfering substance was spiked into non-pregnant pooled urine and 10mIU/ml hCG urine standards.

Each condition was tested with 5 devices from each of three batches of the Clearblue® Early Digital Pregnancy Test for each of the two urine standards according to the dip sampling method. No interference effect was observed at the tested concentration shown in table below:

Interfering Substance	**Concentration**
Acetylsalicylic acid	1.0mg/ml
Acetone	1.0mg/ml
Albumin	5mg/ml
Ampicillin	200 µg/ml

Interfering Substance	Concentration
Ascorbic acid	150µg/ml
Atropine	200 µg/ml
Bilirubin	200 µg/ml
Caffeine	1.2mg/ml
Clomiphene citrate	24µg/ml
Ethanol	1% v/v
Gentistic Acid	200 µg/ml
Glucose	20 mg/ml
Haemoglobin	100µg/ml
Hydrochloric acid	1.25mM
Ibuprofen	100µg/ml
Cotinine	40µg/ml
Oxytetracycline	300µg/ml
Paracetamol (Acetaminophen)	600µg/ml
Phenylpropanolamine	200 µg/ml
Sodium hydroxide	1.25mM
Tetracycline	300µg/ml
Urea	30mg/ml
Uric acid	750µg/ml
Urobilinogen	100µg/ml
E3G	620ng/ml
P3G	40µg/ml
Leukocytes	$1x10^6$ cells/ml
Blood	0.3% v/v
Semen	5% v/v

Structure related compounds

The Clearblue® Early Digital Pregnancy Test devices were tested with 3 potential cross reactants. Each potential cross reactant was spiked into non-pregnant pooled urine and 10mIU/ml hCG urine standard at the following concentration:

Cross Reactant	Concentration
Follicle – Stimulating Hormone (FSH)	1000 mIU/ml
Luteinizing Hormone (LH)	500 mIU/ml
Thyroid – Stimulating Hormone (TSH)	1mIU/ml

No cross reactivity was observed at tested concentration.

Effects of urine pH

Effect of urine pH was performed by adjusting negative and 10mIU/ml hCG urine standard to a pH range of 4, 6 and 9. Each urine standard was tested with 34 devices from each of 3 batches by dip sampling method. The results demonstrated that Clearblue® Early Digital Pregnancy Test will continue to return a correct result when tested with a urine sample in the pH range of 4 – 9.

Effect of urine specific gravity

To test the effect of urine specific gravity, device was challenged with negative (<0.5 mIU/ml hCG) and positive (10mIU/ml hCG) urine standards with the specific gravity of 1.000, 1.007, 1.014, 1.027 and 1.035. The results showed Clearblue® Early Digital Pregnancy Test will continue to return a correct result in response to changes in specific gravity within the range from 1.000 to ≤1.035.

Effect of hCG beta core fragment (hCGβcf)

To evaluate the effect of the hCGβcf, a total of 180 devices were tested:

- Pooled pregnant urine from weeks 6-7 from LMP and negative pooled urine spiked with hCG to a concentration representative of 6-7 weeks pregnant urine samples spiked with 1µM of hCGβcf
- Pooled pregnant urine from weeks 9-12 from LMP and negative pooled urine spiked with hCG to a concentration representative of 9-12 weeks pregnant urine samples spiked with 1µM of hCGβcf
- Non-pregnant pooled urine spiked to 10mIU/ml hCG and 150pmol/L of hCGßcf
- Positive (pooled pregnant urine without spiked hCGβcf) and negative (0mIU/ml) controls were also tested.

Additionally, devices were tested with 30 individual clinical pregnant urine samples collected from late first trimester pregnancies selected as being those with the highest concentrations of hCGβcf.

The results show that the performance of the Clearblue® Early Detection Pregnancy Test is not affected by high concentrations of hCG β-core fragment.

h) Assay cut-off

See Precision/Reproducibility section.

2. Comparison Study

a. Method comparison with predicate device:

102 urine samples from pregnant women and 102 urine samples from not pregnant women were tested by trained technicians using the dipping and simulated in-stream method of sampling across three batches of Clearblue® Early Detection Pregnancy Test. The same samples were also tested using the predicate device FIRST RESPONSE™ Gold Digital Pregnancy Test, using the dip method of sampling.

Clearblue® Early Detection Pregnancy Test had 99.5% agreement with the FIRST RESPONSE™ Gold Digital Pregnancy Test and 100% agreement with the clinical status of the volunteers' urine samples.

b. Matrix comparison:

Not Applicable. The device is intended for urine sample 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)

Detection of hCG in Early Pregnancy Clinical Samples

831 early pregnancy urine samples from days -1 to -10 relative to the day of the missed period were collected. Each sample was tested using both method of sampling across three batches of devices.

The early pregnancy detection results are summarised in table below:

Days Relative to Missed Period	Dip Test results			Simulated In-stream Test Results			Overall Pregnancy Detection
	Not Pregnant (n)	Pregnant (n)	Pregnant (%)	Not Pregnant (n)	Pregnant (n)	Pregnant (%)	
-10	21	0	0.0	21	0	0.0	0.0
-9	36	0	0.0	36	0	0.0	0.0
-8	57	3	5.0	57	3	5.0	5.0
-7	67	35	34.3	62	40	39.2	36.8
-6	25	77	75.5	19	83	81.4	78.4
-5	7	95	93.1	7	95	93.1	93.1
-4	1	101	99.0	1	101	99.0	99.0
-3	0	102	100.0	0	102	100.0	100.0
-2	0	102	100.0	0	102	100.0	100.0
-1	0	102	100.0	0	102	100.0	100.0

Lay User Study

Pregnant and not pregnant women volunteers with diverse educational and professional backgrounds and ages between 18 and 45 years old participated in the Lay User Study. They tested their own sample following both methods of sampling (if they wished to) according to the IFU provided.

The same urine sample was also tested by a technician by dip method only. Volunteer results were compared to their clinical pregnancy status and to the results obtained from trained technicians.

The study confirmed that PPV, NPV, sensitivity, specificity and accuracy for the Clearblue® Early Detection Pregnancy Test in the hands of lay-user volunteers was 100%, for both dip and in-stream testing methods.

The agreement between lay-user volunteer results (in-stream vs dip test) and their clinical status with the Clearblue® Early Detection Pregnancy Test

was 100%. There was also 100% agreement between all lay-user volunteer results and technician dip results.

The results are summarised in tables below:

Volunteer (both in-stream and dip results combined) vs clinical pregnancy status.

		Volunteer Result		
		Not Pregnant	**Pregnant**	**Total**
Clinical Status	**Not Pregnant**	205	0	205
	Pregnant	0	189	189
	Total	205	189	394

Volunteer (In-stream) results and Technician (Dip) Results

		Volunteer In-Stream Result		
		Not Pregnant	**Pregnant**	**Total**
Technician Dip Result	**Not Pregnant**	101	0	101
	Pregnant	0	94	94
	Total	101	94	195

Volunteer and Technician Dip Sampling Method Device Results

		Volunteer Dip Result		
		Not Pregnant	**Pregnant**	**Total**
Technician Dip Result	**Not Pregnant**	104	0	104
	Pregnant	0	95	95
	Total	104	95	199

Specificity study to determine false-positive result rate

A study was performed to determine the incidence of false positive results among non-pregnant women of pre-menopausal age (18-40 years), peri-menopausal age (41-55 years) and post-menopausal age (>55 years).
150 urine samples were collected from individual women of each cohort. All 450 urine samples were tested by technicians with three batches of the Clearblue® Early Digital Pregnancy Test devices by dip method of sampling.

The results are summarised in table below:

Cohort	Not Pregnant (n)	Samples (n)	Specificity (%)
Pre-menopausal	150	150	100.0
Peri-menopausal	150	150	100.0
Post-menopausal	149	150	99.3
All Not Pregnant	449	450	99.8

There was 1 sample from the post-menopausal cohort with a raised hCG concentration that gave a positive result. The hCG concentration of this sample was determined as 7.83 mIU/ml, which is higher than the analytical cut-off of the device.

Lay User Spiked Standard Study

A study was performed to analyse the performance of the Clearblue® Early Digital Pregnancy Test, when read by lay users according to the Instruction for Use. A range of hCG urine standards at 3, 7.5, 8.5, 10 mIU/ml were tested by volunteers representing lay users by both dip and in-stream sampling method.

The overall results when tested by lay users are summarised in table below:

hCG standard (mIU/ml)	Total (n)	Pregnant (n)	Pregnant (%)
3	200	0	0
7.5	200	100	50
8.5	200	148	74
10	200	200	100

5. Clinical Cut-off

Not applicable.

6. Expected value /Reference range

Not applicable.

substantially equivalent to

Conclusion

The conclusions drawn from the nonclinical and clinical tests that demonstrate that the device is ~~as safe, as effective, and performs as well as or better than~~ the legally marketed predicate device: FIRST RESPONSE™ Gold Digital Pregnancy Test (k123567).