September 21, 2022

SPD Swiss Precision Diagnostics GmbH
% Kamila Przedmojska
Principal Regulatory Affairs Specialist
SPD Development Company Limited
Priory Business Park, Stannard Way
Bedford, Bedfordshire MK44 3UP
United Kingdom

Re: K213379
Trade/Device Name: Clearblue® Early Pregnancy Test
Regulation Number: 21 CFR 862.1155
Regulation Name: Human Chorionic Gonadotropin (hCG) Test System
Regulatory Class: Class II
Product Code: LCX
Dated: June 24, 2022
Received: July 5, 2022

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,

Paula Caposino, Ph.D.
Acting Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k213379

Device Name
Clearblue® Early Pregnancy Test

Indications for Use *(Describe)*
The Clearblue® Early Pregnancy Test is an over-the-counter chromatographic immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine. This 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: 24 June, 2022

D. Device Name: Clearblue® Early 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: FIRST RESPONSE™ Early Result Pregnancy Test (k123436)

F. Indication for Use

The Clearblue® Early Pregnancy Test is an over-the-counter chromatographic immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine. This 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 Pregnancy Test is an over-the-counter (OTC), visual pregnancy test 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 test incorporates a proprietary, FSH modulated, hCG scavenger system positioned upstream of the hCG test line to maintain high specificity to pregnancy. The scavenger system captures hCG when there are high levels of FSH in the sample. This ensures that hCG is removed from samples with elevated levels of FSH, reducing the chance of false positive results which while rare, may occur in some women.

The result is displayed to the user in the test window as two lines for a 'Pregnant' result and one line for a 'Not Pregnant' result.

H. Substantial Equivalence Information

Predicate device name:
FIRST RESPONSE™ Early Result Pregnancy Test

Predicate (k) number:
k123436

Comparison with predicate:

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

Component	Clearblue® Early Pregnancy Test (Proposed Device)	FIRST RESPONSE™ Early Result Pregnancy Test (Predicate Device)
Similarities		
Intended Use	Qualitative detection of human hCG for an aid in early detection of pregnancy	Same
'Early Test' Claim	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
Target User	Over-The-Counter use	Same
Device format	Single Use	Same
Sample Matrix	Urine	Same
Analyte	hCG	Same
Sample application	In-stream and dip	Same
hCG Sensitivity	10mIU/ml	Same
Traceability	WHO 4th International Standard for hCG	Same
Test Principle	Lateral flow sandwich immuno-chromatographic assay	Same
Assay Mobile Phase	Gold conjugate	Same
Test Type	Qualitative	Same
Control Mechanism	Visual	Same
Results Display	Visual Parallel Line 2 Lines = Pregnant 1 Line = Not Pregnant	Same
Differences		
Analyte Detection	Detects intact hCG. Scavenger system to remove intact hCG in the presence of FSH.	Recognises: intact hCG hyperglycosylated hCG hCG β-subunit hCG β-core fragment
Time to results	5 minutes	3 minutes

I. Test Principle

The Clearblue® Early 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 Clearblue® Early Pregnancy 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.

Buffer salts in the wick are dissolved by the sample, normalising the pH and ionic strength to provide suitable conditions for the down-stream immunoassay. Upon wetting of the wick, urine is drawn by capillary action into the conjugate pad. As the sample moves from the wick through the conjugate release pad, the antibody coated gold-sol particles are mobilized and transported along the test strip. Any hCG and/or FSH in the sample will bind to the test gold-sol label via their common alpha sub-unit.

On reaching the nitrocellulose membrane, the sample is drawn across the plotted line of immobilised anti-beta FSH antibody in the scavenger zone which is not visible to the user as it is located within the plastic case moulding. The sample then progresses across the monoclonal anti-beta hCG antibody test line and polyclonal anti-rabbit antibody control line and on to the distal end of the test strip into the sink pad.

J. Performance characteristics

1. Analytical Performance

a) Precision/Reproducibility

1. A not-pregnant pooled urine was spiked with hCG traceable to the 4th WHO international standard with hCG concentrations of <1, 2, 3, 5, 7, 10, 15 and 20 mIU/ml. Each standard was tested with devices from three different batches using both dip and simulated in-stream sampling methods. The study was performed by three technicians over five non-consecutive days.

The results are summarised in the tables below:

Overall Precision Results of Clearblue® Early Pregnancy Test

hCG Standard (mIU/ ml)	Clearblue® Early 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 (%)	
<1	135	0	0.0	135	0	0.0	0.0
2	135	0	0.0	135	0	0.0	0.0
3	102	33	24.4	100	35	25.9	25.2
5	43	92	68.1	42	93	68.9	68.5
7	16	119	88.1	18	117	86.7	87.4
10	0	135	100.0	0	135	100.0	100
15	0	135	100.0	0	135	100.0	100
20	0	135	100.0	0	135	100.0	100

Percentage Pregnant Results for Each hCG Standard by Technician

hCG Standard (mIU/ ml)	Technician 1		Technician 2		Technician 3	
	Pregnant/ Not Pregnant (n)	Pregnant Results (%)	Pregnant/ Not Pregnant (n)	Pregnant Results (%)	Pregnant/ Not Pregnant (n)	Pregnant Results (%)
<1	0/90	0.0	0/90	0.0	0/90	0.0
2	0/90	0.0	0/90	0.0	0/90	0.0
3	21/69	23.3	23/67	25.6	24/66	26.7
5	59/31	65.6	62/28	68.9	64/26	71.1
7	77/13	85.6	78/12	86.7	81/9	90.0
10	90/0	100	90/0	100	90/0	100
15	90/0	100	90/0	100	90/0	100
20	90/0	100	90/0	100	90/0	100

Percentage Pregnant Results for Each hCG standard by Batch

hCG Standard (mIU/ ml)	Batch 1		Batch 2		Batch 3	
	Pregnant/ Not Pregnant (n)	Pregnant Results (%)	Pregnant/ Not Pregnant (n)	Pregnant Results (%)	Pregnant/ Not Pregnant (n)	Pregnant Results (%)
<1	0/90	0.0	0/90	0.0	0/90	0.0
2	0/90	0.0	0/90	0.0	0/90	0.0
3	25/65	27.8	22/68	24.4	21/69	23.3
5	63/27	70.0	63/27	70.0	59/31	65.6
7	79/11	87.8	80/10	88.9	77/13	85.6
10	90/0	100	90/0	100	90/0	100
15	90/0	100	90/0	100	90/0	100
20	90/0	100	90/0	100	90/0	100

Percentage Pregnant Results for Each hCG standard by Day

hCG Standard (mIU/ ml)	Day 1		Day 2		Day 3		Day 4		Day 5	
	P/NP (n)	Pregnant Results (%)	P/NP (n)	Pregnant Results (%)	P/NP (n)	Pregnant Results (%)	P/NP (n)	Pregnant Results (%)	P/NP (n)	Pregnant Results (%)
<1	0/54	0.0	0/54	0.0	0/54	0.0	0/54	0.0	0/54	0.0
2	0/54	0.0	0/54	0.0	0/54	0.0	0/54	0.0	0/54	0.0
3	14/40	25.9	14/40	25.9	11/43	20.4	15/39	27.8	14/40	25.9
5	39/15	72.2	36/18	66.7	37/17	68.5	35/19	64.8	38/16	70.4
7	47/7	87.0	49/5	90.7	46/8	85.2	44/10	81.5	50/4	92.6
10	54/0	100	54/0	100	54/0	100	54/0	100	54/0	100
15	54/0	100	54/0	100	54/0	100	54/0	100	54/0	100
20	54/0	100	54/0	100	54/0	100	54/0	100	54/0	100

b) Linearity/assay reportable range:

Not applicable. This is a qualitative device.

c) High dose hook effect study:

A not-pregnant pooled urine was spiked with hCG to concentrations of <1, 10, 10,000 and 1,000,000mIU/ml and tested with 5 replicates from each of three batches. No hook effect was observed at the tested concentrations.

d) Traceability

The tests are calibrated against the WHO 4th International Standards for human 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

Structurally not-related compounds

Interfering substances
The Clearblue® Early Pregnancy Test devices were tested with potential 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 Pregnancy Test for each of the two urine standards according to the dip sampling method. No interference effect was observed at the tested concentrations shown in the table below:

Interfering Substance	Concentration
Acetylsalicylic acid	1.0mg/ml
Acetone	1.0mg/ml
Albumin	5mg/ml
Ampicillin	20 mg/dL
Ascorbic acid	150µg/ml
Atropine	200 µg/mL
Bilirubin	20 mg/dL
Blood	0.3% v/v
Caffeine	1.2mg/ml
Cannibinol	10 mg/dL
Clomiphene citrate	24µg/ml
Cotinine	40 µg/ml
Ethanol	1% v/v
E3G	620ng/ml
Gentisic acid	20 mg/dL
Glucose	20mg/ml
Haemoglobin	100µg/ml
Hydrochloric acid	1.25mM
Ibuprofen	100µg/ml
Leukocytes	x106 cells/ml
Oxytetracycline	300µg/ml
Paracetamol (Acetaminophen)	600µg/ml
Phenylpropanolamine	20 mg/dL
P3G	40µg/ml
Semen	5% v/v
Sodium hydroxide	1.25mM
Tetracycline	300µg/ml
Urea	30mg/ml
Uric acid	750µg/ml
Urobilinogen	100µg/ml

Structurally related compounds

Effects of cross reactants

The results in the table below show that all the devices tested returned the correct result when tested with potential cross reactants at the concentrations shown below.

Standards	Result		Pass/Fail
	Pregnant (n)	Not Pregnant (n)	
<1 hCG mIU/ml	0	15	Pass
10 hCG mIU/ml	15	0	Pass
<1 hCG mIU/ml, 500 LH mIU/ml	0	15	Pass
10 hCG mIU/ml, 500 LH mIU/ml	15	0	Pass
<1 hCG mIU/ml, 1 TSH mIU/ml	0	15	Pass
10 hCG mIU/ml, 1 TSH mIU/ml	15	0	Pass
<1 hCG mIU/ml, 1000 FSH mIU/ml	0	15	Pass
10 hCG mIU/ml, 15 FSH mIU/ml	15	0	Pass
4 hCG mIU/ml, 100 FSH mIU/ml	0	30	Pass
4 hCG mIU/ml, 1000 FSH mIU/ml	0	30	Pass
4 hCG mIU/ml, 100 FSH mIU/ml, 1 TSH mIU/ml	0	30	Pass
4 hCG mIU/ml, 100 FSH mIU/ml, 500 LH mIU/ml	0	30	Pass

Effects of urine pH

Effect of urine pH was performed by adjusting negative (<1 mIU/ml) and 10mIU/ml hCG urine standards to a pH range of 4, 6 and 9. Each urine standard was tested with 5 devices from each of 3 batches by dip sampling method. The results demonstrated that Clearblue® Early 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 specific gravity, the device was challenged with non-pregnant pooled urine and positive (10mIU/ml hCG) urine standards with specific gravity of 1.000, 1.01, 1.015, 1.03 and 1.035. Each urine standard

was tested with 5 devices from each of 3 batches by dip sampling method. The results showed the Clearblue® Early 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 hCGβcf, 11 conditions were tested with 5 devices from each of 3 batches, totalling 165 devices.

Pooled pregnant urine collected from 6-7 weeks and 9-12 weeks pregnancy were tested with and without hCGβcf spiked up to 1μM.

Pooled negative urine spiked with hCG to a concentration representative of 6-7 weeks and 9-12 weeks pregnant urine samples were tested with and without hCGβcf spiked up to 1μM.

A non-pregnant pooled urine was spiked to 10mIU/ml hCG then spiked with 150pM hCGβcf (a concentration 5 times the molar concentration of intact hCG) was tested. Positive (negative pooled urine spiked to 10mIU/ml) and non-pregnant (<1.0 mIU/ml) controls were also tested.

The results show that the performance of the Clearblue® Early 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:

The Lay User Usage study collected the lay users and technician results and compared them against physician determined clinical pregnancy status, hence the comparison to the predicate device was not performed.

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

Early pregnancy urine samples from days -10 to 0 relative to the day of the missed period were collected. Each sample was tested using both methods of sampling across three batches of devices.

The early pregnancy detection results are summarised in table below:

Day Relative to Missed Period	Total Samples (n)	Number Pregnant Result (n)	Percent Pregnant Result (%)
-10	42	0	0.0
-9	72	0	0.0
-8	120	6	5.0
-7	204	58	28.4
-6	204	158	77.5
-5	204	191	93.6
-4	204	200	98.0
-3	204	204	100
-2	204	204	100
-1	204	204	100
0	204	204	100

Lay User Study

Pregnant and not pregnant women volunteers with diverse educational and professional backgrounds and ages between 18 and 55 years old participated in the Lay User Usage Study. Their results were compared to their clinical pregnancy status and to the results obtained from trained technicians testing the same urine samples in the same sampling method (either simulated in-stream or dipping).

The study confirmed that PPV, NPV, sensitivity, specificity and accuracy for the Clearblue® Early 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 and their clinical status with the Clearblue® Early Pregnancy Test was 100%. There was also 100% agreement between all lay-user volunteer results and technician results.

The results are summarised in tables below:

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

Clinical Pregnancy Status	Volunteer Result		
	Pregnant	Not Pregnant	Total
Pregnant	152	0	152
Not Pregnant	0	143	143
Total	152	143	295

Volunteer (In-stream) results vs clinical pregnancy status

Clinical Pregnancy Status	Volunteer Result		
	Pregnant	Not Pregnant	Total
Pregnant	59	0	59
Not Pregnant	0	57	57
Total	59	57	116

Volunteer (Dip) results vs clinical pregnancy status

Clinical Pregnancy Status	Volunteer Result		
	Pregnant	Not Pregnant	Total
Pregnant	93	0	93
Not Pregnant	0	86	86
Total	93	86	179

Volunteer results vs technician result

Technician Test Results	Volunteer Result		
	Pregnant	Not Pregnant	Total
Pregnant	152	0	152
Not Pregnant	0	143	143
Total	152	143	295

Lay User Spiked Standard Study

A study was performed to analyse the performance of the Clearblue® Early Pregnancy Test when read by lay user according to the Instructions for Use. A range of the hCG urine standards at 0, 2, 3, 5, 10 and 15mIU/ml were sampled by dip method of sampling and read by lay users. The results are shown in table below:

hCG Standard (mIU/ml)	Total (n)	Number Pregnant (n)	Percent Pregnant (%)
0	107	0	0.0
2	107	2	1.9
3	103	28	27.2
5	106	74	69.8
10	105	105	100
15	108	108	100

Specificity study to determine false-positive result rate

A study was performed to determine the incidence of false positive results among not-pregnant women of pre-menopausal age (18-40 years), peri-menopausal age (41-55 years) and post-menopausal age (>55 years). Urine samples were collected from individual women of each cohort and were tested by technicians with three batches of the Clearblue® Early Pregnancy Test devices by both dip and simulated in-stream method of sampling.

The results (combined method of sampling) are summarised in table below:

Cohort	Not Pregnant (n)	Samples (n)	Specificity (%)
Pre-menopausal	300	300	100
Peri-menopausal	299	299	100
Post-menopausal	300	300	100
All Not Pregnant	899	899	100

Clinical Cut-off

Not applicable.

Expected value /Reference range

Not applicable.

K. Conclusion

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