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

A. 510(k) Number:

k123436

B. Purpose for Submission:

Modification of device (change in hCG antibody)

C. Measurand:

Human chorionic gonadotropin (hCG)

D. Type of Test:

Qualitative chromatographic immunoassay

E. Applicant:

Church and Dwight Co., Inc.

F. Proprietary and Established Names:

FIRST RESPONSE® Early Result Pregnancy Test

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 FIRST RESPONSE® Early Result Pregnancy Test is an over-the-counter chromatographic immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine. The device is intended for use as an aid in early detection of pregnancy, in some cases as early as five (5) days before the expected period, i.e., as early as six (6) days before the day of the missed period.

Important note regarding negative results:
Some pregnant women will not be able to detect hCG in their urine 5 days before the expected period. If you test negative before your missed period, but think you may still be pregnant, you should test again a few days after your missed period.

Important note regarding positive results:
Because this test detects low levels of hCG, it is possible that this test may give positive results even if you are not pregnant. If you test positive, but think you may not be pregnant, you should check with your doctor.

All results should be confirmed by your healthcare provider, especially when making decisions about future medical care.

3. Special conditions for use statement(s):

   For over the counter use

4. Special instrument requirements:

   None

I. Device Description:

The FIRST RESPONSE® Early Result Pregnancy Test is a screening device intended for the early detection of pregnancy by the lay user through the qualitative detection of human chorionic gonadotropin (hCG) hormone in urine, in some cases as early as 5 days before the expected period. The device consists of a chromatographic test strip enclosed in plastic housing and the package insert. The test strip contains streptavidin-biotin chemistry, mouse monoclonal and goat anti-mouse polyclonal antibodies. The test result is displayed at the housing window for reading by the lay user after the elapse of 3 minutes. Two pink lines indicate that hCG has been detected (pregnant); one pink line indicates that no hCG has been detected (not pregnant).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   FIRST RESPONSE® Early Result Pregnancy Test

2. Predicate K number(s):

   k083716

3. Comparison with predicate:

Similarities		
Feature	**Candidate Device**	**Predicate Device**
Intended Use	Early detection of pregnancy	Same
Target User	Over-the-Counter Use	Same
Sample Matrix	Urine	Same
Device Format	Midstream or dip mode	Same
Test Principle	Lateral flow sandwich immunochromatographic assay	Same
Time to Result	3 minutes	Same
Shelf life	24-month shelf life when stored in a dry place below 86ºF	Same
Differences		
Feature	**Candidate Device**	**Predicate Device**
hCG isoforms detected	intact hCG hyperglycosylated hCG hCG β-subunit hCG β-core fragment	intact hCG hyperglycosylated hCG hCG β-subunit

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

None were referenced

L. Test Principle:

This device operates by detecting hCG (and its isoforms), the hormone produced during pregnancy, using a lateral flow sandwich immunochromatographic assay.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Six urine standards containing intact hCG at concentrations of 0, 3, 6, 10, 15, 25 mIU/mL were prepared in negative urine pools and calibrated against the WHO 4th International Standard (IS) for hCG. Five lots of devices were tested according to package insert instructions with each of the hCG standards in replicates of 10. Testing was performed for three consecutive days by different technicians each day. A total of 30 results per lot per level were obtained. The cumulative results are summarized in the table below.

hCG concentration	Lot# 1	Lot# 2	Lot# 3	Lot# 4	Lot# 5	% positive
0 mIU/mL	30/30 negative	30/30 negative	30/30 negative	30/30 negative	30/30 negative	0%
3 mIU/mL	30/30 negative	30/30 negative	30/30 negative	30/30 negative	30/30 negative	0%
6 mIU/mL	15/30 positive	13/30 positive	14/30 positive	13/30 positive	15/30 positive	47%
10 mIU/mL	30/30 positive	30/30 positive	30/30 positive	30/30 positive	30/30 positive	100%
15 mIU/mL	30/30 positive	30/30 positive	30/30 positive	30/30 positive	30/30 positive	100%
25 mIU/mL	30/30 positive	30/30 positive	30/30 positive	30/30 positive	30/30 positive	100%

b. Linearity/assay reportable range:

Linearity is not applicable since this is a qualitative test.

The high dose effect was evaluated using intact hCG standards (WHO 4th IS) ranging from 0.1 to 500 IU/mL hCG concentrations, and hCG βcf at 500,000 and 1,000,000 pmol/L levels. All samples yielded the expected positive results.

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

The test is calibrated against the WHO 4th IS for hCG.

The stability testing protocol and acceptance criteria used to support the shelf life were reviewed and found to be acceptable. The sponsor claims a 24-month shelf life for the test when stored below 86ºF (30ºC).

d. Detection limit:

Urine standards containing intact hCG at concentrations of 0, 3, 6, 10, 15, 25 mIU /mL were prepared in negative urine pool and calibrated against the WHO 4th IS for hCG. Each standard was tested in replicates of 20 with three lots of the new device using the dip method, and with one lot of the new device using a simulated midstream method. The results are summarized in the table below:

hCG concentration	Dip mode			Midstream
	Lot #1	Lot #2	Lot #3	Lot #4
0 mIU/mL	20/20 negative	20/20 negative	20/20 negative	20/20 negative
3 mIU/mL	20/20 negative	20/20 negative	20/20 negative	20/20 negative
6 mIU/mL	10/20 positive	8/20 positive	9/20 positive	9/20 positive
10 mIU/mL	20/20 positive	20/20 positive	20/20 positive	20/20 positive
15 mIU/mL	20/20 positive	20/20 positive	20/20 positive	20/20 positive
25 mIU/mL	20/20 positive	20/20 positive	20/20 positive	20/20 positive

The results demonstrated that the analytical sensitivity of the new device (the lowest concentration that yields 100% positive results) is 10 mIU/mL and the cut-off level (at which approximately half of the devices yield positive results and the remainder yield negative results) is 6 mIU/mL.

e. Analytical specificity:

Various prescription and OTC drugs (acetaminophen, acetylsalicylic acid, ascorbic acid, ampicillin, atropine, caffeine, gentisic acid, phenothiazine, phenylpropanolamine and tytracycline, all at 10 µg/mL), potential endogenous interferents (glucose and albumin at 20 mg/mL, hemoglobin, bilirubin, and estriol at 10 µg/mL) and homologous hormones (hLH and hFSH at 1000 mIU/mL, hTSH at 1 mIU/mL) were added to aliquots of urine pools that tested negative for hCG and urine pools that contained hCG at 10mIU/mL. Samples were tested in replicates of 10. No affects on test performance were observed.

f. Assay cut-off:

See detection limit section above.

2. Comparison studies:

a. Method comparison with predicate device:

The performance of the new device was compared to the predicate test of the same name, FIRST RESPONSE® Early Result Pregnancy Test by laboratory technicians. A total of 600 urine samples were randomized and masked and tested with one lot of the predicate device and three lots of the new device. The results are summarized below.

Candidate Device	Predicate Device		
		+	-
	+	300	0
	-	0	300

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):

Detection of hCG in Early Pregnancy Clinical Samples

A total of 454 urine samples from 50 characterized cycle segments of conceptive cycles collected from 50 different pregnant women were tested by a laboratory technician. Urine samples were masked and randomized. Each urine sample was tested with one device selected from three device lots according to a randomization table.

The new device detected hCG in 76% of the cycles five days before the expected menstrual period and in 100% of the cycles on the day of the expected menstrual period. The sensitivity of the new device with patient samples is consistent with that of the predicate device. The following table summarizes detection of hCG with the new device relative to the day of the expected menstrual period (EMP) for the conceptive cycles tested.

Detection of hCG in Conceptive Cycles Relative to Day of Expected Menstrual Period (EMP) and Day of luteinizing hormone (LH) peak using new device

Day relative to EMP	EMP-11	EMP-10	EMP - 9	EMP - 8	EMP-7	EMP-6	EMP-5	EMP-4	EMP-3	EMP-2	EMP-1	EMP
Day relative to LH Peak	LH + 4	LH + 5	LH + 6	LH + 7	LH + 8	LH + 9	LH + 10	LH + 11	LH + 12	LH + 13	LH + 14	LH + 15
# of cycles positive for hCG	0/2	0/8	1/18	3/35	9/45	23/48	38/50	47/49	50/50	50/50	49/49	50/50
Cumulative % cycles positive for hCG	0%	0%	6%	9%	20%	48%	76%	96%	100%	100%	100%	100%

Note: EMP was calculated by adding 15 days to the day with the highest quantitative urinary concentration of luteinizing hormone (LH), i.e., day of LH peak plus 15 days (LH+15).

Lay user study

The sponsor performed two studies with lay user consumers:

In the first study, one hundred and two female subjects (89 non-pregnant and 13 pregnant) between the ages of 18 and 45 were recruited. The devices used in this study were randomized from three lots prior to use by the lay users. Of the total number of participants, 69 (68%) performed the test in mid-stream and the remainder 33 (32%) used the dip method. Consumer interpretation of results compared to lab technicians are tabulated below.

Result	Number of samples	Consumer vs. Technicians
Pregnant	13	13/13 (100%)
Non-pregnant	89	89/89 (100%)
Total	102	102/102 (100%)

In the second study, forty eight lay users were recruited to interpret test results from masked samples containing varying concentrations of intact hCG using three lots of new devices. The results are summarized in the table below:

hCG concentration	Lot #1	Lot #2	Lot #3
0 mIU/mL	16/16 negative	16/16 negative	16/16 negative
3 mIU/mL	14/16 negative	16/16 negative	16/16 negative
6 mIU/mL	8/16 positive	10/16 positive	7/16 positive
10 mIU/mL	16/16 positive	16/16 positive	15/16 positive
15 mIU/mL	16/16 positive	16/16 positive	16/16 positive
25 mIU/mL	16/16 positive	16/16 positive	16/16 positive

A few positive samples were detected at a low hCG concentration (3 mIU/mL). The labeling states that it is possible that this test may give positive results even if the user is not pregnant. Users are instructed to check with their doctor if they test positive, but think they may not be pregnant.

All lay users were instructed to read the proposed package insert (in English) to operate the device for the studies above. Each lay user was also given a questionnaire to rate how well they understood the instructions. All lay users agreed that the user instruction was written in a manner that was easy to use and understand.

Non-pregnant urine sample analysis

A study was performed to determine the incidence of positive results in urine from non-pregnant females when tested with the candidate device. Urine specimens from non-pregnant women in pre-menopausal (ages 18-40), peri-menopausal (41-55 years) and post-menopausal (>55 years) age groups were evaluated. No pre-selection or pre-screening based on hCG was performed prior to testing with three (3) lots of devices. The results are summarized in the table below.

Age Group	Urine specimens (N)	Positive results (%)
18-40 years old	102	0/102 (0%)
41-55ears old	102	0/102 (0%)
>55 years old	102	1/102 (0.98%)

4. Clinical cut-off:

   Not applicable

5. Expected values/Reference range:

   Not applicable

N. Proposed Labeling:

The labeling is sufficient and it does satisfy 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.