510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

K131166

B. Purpose for Submission:

New device

C. Measurand:

Human chorionic gonadotropin (hCG) in human urine

D. Type of Test:

Qualitative fluorescent immunoassay

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Sofia® hCG FIA

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JHI	Class II	21 CFR§ 862.1155, Human chorionic gonadotropin (HCG) test system	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See below

2. Indication(s) for use:

   The Sofia hCG FIA is an immunofluorescence-based lateral flow assay intended for the qualitative detection of human Chorionic Gonadotropin (hCG) in urine specimens for the early detection of pregnancy.

   The test is intended for prescription use only, including use at point-of-care sites.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   For use with the Sofia Analyzer

I. Device Description:

The test kit consists of individually packaged test Cassettes—each containing mouse monoclonal anti-hCG antibodies for the capture and detection of hCG; disposable specimen transfer pipettes; and a package insert.

J. Substantial Equivalence Information:

1. Predicate Device Name:

   CARDS® Q.S.® hCG Serum/Urine and Concise Performance Plus hCG-Combo

2. Predicate 510(k) Number:

   K973858

3. Comparison with Predicate:

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Item	Predicate Device	Candidate Device
Features	CARDS® Q.S.® hCG Serum/Urine and Concise Performance Plus hCG-Combo **(K973858)**	**Sofia hCG FIA**
Intended Use	The QuickVue+ One-Step hCG Combo test is a one-step immunoassay intended for the qualitative detection of human Chorionic Gonadotropin (hCG) in serum or urine for the early detection of pregnancy. The test is intended for use by healthcare professionals	. Same
Specimen Type	Urine/Serum	Urine
Format	Cassette	Same
Test Principle	Lateral flow immunoassay	Same
Instrument	No instrument; visually-read assay	Sofia Analyzer
Read Result Time	3 minutes	Same for urine
Analytical Sensitivity	20 mIU/mL for urine	Same for urine
Storage	15 to 30°C	Same

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

1. CLSI EP 5 A2: A Evaluation of Precision Performance of Quantitative MeasurementMethods; Approved Guideline—Second Edition 08/20/2004

2. CLSI EP 7A2 : Interference Testing in Clinical Chemistry; Approved Guideline -Second Edition 11/23/2005

3. CLSI EP 12 A2: User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline - Second Edition 01/25/2008

4. CLSI EP 25A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline - 09/23/2009

5. CLSI LS101 A2 : Specification for Low-Level Protocol to Transfer Messages Between Clinical Laboratory Instruments and Computer Systems; Approved Standard—Second Edition 04/28/2008

6. CLSI LS102 A2: Specification for Transferring Information Between Clinical Instruments and Computer Systems; Approved Standard—Second. Second Edition 10/20/2004

7. CENELEC. EN 61326-1 Electrical equipment for measurement, control and laboratory use -EMC requirements - Part 1: General requirements 12/2006

8. CENELEC EN 61326-2-6 Electrical equipment for measurement, control and laboratory use. EMC requirements. Particular requirements. Invitro diagnostic (IVD) medical equipment 12/2006

9. IEC 61010-1 Safety requirements for electrical equipment for measurement, control, and laboratory use –Part 1: General requirements 02/2001
10. IEC 61010-2-081 Safety requirements for electrical equipment for measurement, control and laboratory use –Part 2-081: Particular requirements for automatic and semi-automatic laboratory equipment for analysis and other purposes 08/2009

11. IEC 61010-2-101 Safety requirements for electrical equipment for measurement, control, and laboratory use -- Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment 12/2002

12. IEC 62304 Medical device software – Software life-cycle processes 8/20/2012

13. ISO 14971 Medical Devices - Application of risk management to medical devices 08/20/2012

14. ISO 15223-1 Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied —Part 1: General requirements 07/01/2012

L. Test Principle:

The Sofia hCG FIA is an immunofluorescence-based lateral flow test for use with the Sofia Analyzer. The test uses a pair of monoclonal murine antibodies specific to the beta subunit of hCG to capture and detect hCG.

To perform the test, a urine specimen is collected and dispensed into the Sample Well on the Test Cassette. The Cassette is placed inside of the Sofia Analyzer for an automatically defined development time. The Sofia Analyzer then scans the test strip and analyzes the fluorescent signal, using method-specific algorithms. The Sofia Analyzer then displays the

test result (Positive, Negative, or Invalid) on the screen, and optionally prints the results on an integrated printer.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:
   The reproducibility of the Sofia hCG FIA was evaluated at three (3) different laboratories. Three (3) different operators at each site tested a series of coded, four contrived samples, prepared in negative urine, spiked with hCG traceable to WHO International 4th standard to generate samples ranging from 5 mIU/mL to 25 mIU/mL hCG.

   A total of nine (9) Sofia Analyzers were used. For each level a total of 90 replicates were tested over five (5) different days at each site. The results are summarized as follows:

Site	**Operator**	**(5 mIU/mL)**	**(9.5 mIU/mL)**	**(16 mIU/mL)**	**(25 mIU/mL)**
		Negative/Total	Negative/Total	Positive/Total	Positive/Total
1	1	30/30	28/30	29/30	30/30
	2	30/30	30/30	28/30	30/30
	3	30/30	29/30	27/30	30/30
	Total	**90/90**	**87/90**	**84/90**	**90/90**
2	1	30/30	28/30	28/30	30/30
	2	30/30	29/30	29/30	30/30
	3	30/30	29/30	27/30	30/30
	Total	**90/90**	**86/90**	**84/90**	**90/90**
3	1	30/30	26/30	30/30	30/30
	2	30/30	23/30	30/30	30/30
	3	30/30	27/30	29/30	30/30
	Total	**90/90**	**76/90**	**89/90**	**90/90**
Total:		**270(-)/270 Total**	**249(-)/270 Total**	**257(+)/270 Total**	**270(+)/270 Total**

b. Linearity/assay reportable range:

Not applicable. This is a qualitative test.

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

The Sofia hCG FIA is standardized to the WHO Fourth International Standard 75/589.

All stability protocols were reviewed and found to be acceptable. The shelf-life stability study showed that the device is stable for 24 months when stored at room temperature (15 to 30˚C).

d. Detection limit:

The sensitivity of the Sofia hCG FIA was tested by spiking pooled male urine with varying concentrations (0 to 100 mIU/mL) of hCG traceable to WHO International 4th Standard. Studies were conducted with 3 lots of devices. Representative results are listed in the table below. The positive/negative threshold at which 100% of the samples tested positive was confirmed at 20 mIU/mL hCG.

Detection Limit Testing

hCG Conc. (mIU/mL)	Number of Positives	Number of Negatives	Percent Positive
100	10/10	0/10	100%
50	10/10	0/10	100%
30	10/10	0/10	100%
25	60/60	0/60	100%
22.5	60/60	0/60	100%
20	60/60	0/60	100%
17.5	57/60	3/60	95%
15	48/60	12/60	80%
12.5	27/60	33/60	45%
10	5/60	55/60	8.3%
7.5	0/60	60/60	0%
5	0/60	60/60	0%
2.5	0/10	10/10	0%
0	0/10	10/10	0%

e. Analytical specificity:

A hCG negative urine pool was initially spiked with each of the substances listed in the table below. Immediately prior to testing, five (5) levels of hCG (0, 5, 10, 20 and 25 mIU/mL) were then spiked into each solution containing the possible interfering or cross-reacting substance. Urinary pH and specific gravity was also evaluated. All samples were tested in replicates of five (5). The following compounds did not interfere with the test at the following tested concentrations.

Item	Substance/Microorganism	Concentration
1	Acetaminophen	20 mg/dL
2	Acetoacetic Acid	1,600 mg/dL
3	Acetylsalicylic Acid	20 mg/dL
4	Ampicillin	2 mg/dL
5	Ascorbic Acid	20 mg/dL
6	Atropine	20 mg/dL
7	β-Hydroxybutyrate	2,000 mg/dL
8	Benzoylecgonine	8 mg/dL
9	Bovine Serum	10 mg/dL
10	Caffeine	20 mg/dL
11	Cannabinol	10 mg/dL
12	Cellulose	500 mg/dL
13	Citric Acid	500 mg/dL
14	Clomiphene	100 mg/dL
15	Cow's Milk	9 mg/dL
16	DMSO	0.90%
17	EDTA	80 mg/dL
18	Ephedrine	18 mg/dL
19	Ethanol	0.80%
20	Gentisic Acid	20 mg/dL
21	Methanol	0.90%
22	Phenothiazine	20 mg/dL
23	Phenylpropanolamine	20 mg/dL
24	Salicylic Acid	20 mg/dL
25	Tetracycline	20 mg/dL

Item	Substance/Microorganism	Concentration
26	Theophylline	20 mg/mL
27	Uric Acid	18 mg/dL
28	Albumin (serum)	2,000 mg/dL
29	Bilirubin	1 mg/dL
30	Glucose	2,000 mg/dL
31	Haptoglobin	1 mg/dL
32	Hemoglobin	1 mg/dL
33	Human Anti-Mouse Antibodies	2.85 ng/mL
34	Myoglobin	1 mg/dL
35	Rheumatoid Factor	1.08 IU/mL
36	Serum (negative human)	1%
37	Urine Peroxide	10 mg/dL
38	Urine pH	5–9
39	Urine Specific Gravity	1.005-1.037
40	hLH	450 mIU/mL
41	hFSH	900 mIU/mL
42	hTSH	1,000 mIU/mL
43	Estriol 17-beta	28,000 µg/dL
44	Pregnanediol glucuronide	45,000 µg/dL
45	Beta-core fragment, hCG	5.1×10^5 pmol/L

A high dose hook effect study was performed by spiking high levels of hCG concentrations 0 to 500,000 mIU/mL into negative urine and evaluating the test results. Positive results were observed up to 500,000 mIU/mL hCG. Therefore no hook effect was observed for urine samples with hCG concentrations up to 500,000 mIU/mL.

f. Assay cut-off:

Not applicable

2. Comparison studies:

   a. *Method comparison with predicate device:*
   A multi-center clinical study was conducted to establish the performance of the Sofia hCG FIA compared to results obtained from the predicate device. This study was conducted by health care personnel at five (5) different sites within the United States. In this multi-center, point-of-care (POC) field trial, 974 fresh urine specimens, collected from patients presenting for pregnancy testing, were evaluated. The study consisted of female subjects of childbearing age, who were being screened for pregnancy and who had given verbal consent to participation. The following subjects were excluded: post-menopausal subjects, subjects who within the past six weeks had experienced any of the following: delivered a newborn, had an abortion or a natural termination (miscarriage), or, received hCG supplements, subjects who had a hysterectomy, and subjects who were unable to understand and consent to participation. Results from the study are summarized below.

	Predicate	
	Pos	Neg
Sofia Pos	176	2
Sofia Neg	1	795
Total	177	797

   Three discrepant results were from samples collected from patients that were too early in gestational age to obtain comparable results on the candidate and predicate devices.

   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):*

   Not applicable

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Not applicable

N. Instrument Name:

Sofia analyzer.

O. System Descriptions:

1. Modes of Operation:
   The Sofia Analyzer is a bench top instrument intended to be used with cassette based immunofluorescent *in vitro* diagnostic assays manufactured by Quidel Corporation. After the extracted patient sample has been added to the test cassette, the test is developed at room temperature for a pre-specified period of time. The cassette is then placed into the Analyzer where it is scanned, and the fluorescent signal of the test is processed.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ____X____ or No _____

3. Specimen Identification:

   The user ID, patient ID, and order # can be entered via a handheld barcode scanner or by manually entering the information onto the keypad of the Sofia Analyzer.

4. Specimen Sampling and Handling:

   Urine specimen is collected in a clean container. First morning specimens generally contain the highest concentrations of hCG and are recommended for early detection of pregnancy. However, any urine sample is suitable for testing.

   Labeling states that if testing will not be performed immediately, the specimens may be kept at room temperature (15-30°C) or refrigerated (2-8°C) for up to 72 hours. For prolonged storage, specimens may be frozen once at -20°C or below.

5. Calibration:

   The labeling provides details regarding the Calibration Check Procedure for the Sofia

analyzer. The Calibration Check Procedure should be performed every thirty (30) days. The Sofia Analyzer can be set to remind the user to complete the Calibration Check Procedure.

The Calibration Check is a required function that checks the Sofia Analyzer optics and calculation systems using a specific Calibration Cassette. This Calibration Cassette is shipped with the Sofia Installation Pack.

6. Quality Control:

Built-in Procedural Controls

The Sofia hCG FIA test strip contains a built-in procedural control feature. Each time a test is run, the Sofia Analyzer scans this part of the test strip, and the result is displayed on the Analyzer screen as "valid" or "invalid."

A valid result obtained with this procedural control demonstrates that the test flowed correctly and the functional integrity of the Cassette was maintained. The procedural control is interpreted by the Sofia Analyzer simultaneously with the end of the assay. If the test does not flow correctly, the Sofia Analyzer will indicate that the result is invalid. Should this occur, the labeling instructs the user to review the procedure and repeat the test with a new test Cassette.

External Quality Control

External controls are also recommended for use to demonstrate that the reagents and assay procedure perform properly. Labeling recommends that controls be tested once for each new lot, new shipment of kits, and every 30 days as a check on storage and if applicable, as deemed additionally necessary by laboratory internal quality control procedures, and in accordance with local, state and federal regulations or accreditation requirements.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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