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

**A. 510(k) Number:**

K131037

**B. Purpose for Submission:**

New Device

**C. Measurand:**

Human chorionic gonadotropin

**D. Type of Test:**

Quantitative Chemiluminescent Immunoassay

**E. Applicant:**

DIASORIN, INC

**F. Proprietary and Established Names:**

LIAISON® XL HCG

**G. Regulatory Information:**

| Product Code | Classification | Regulation Section | Panel |
|---|---|---|---|
| DHA | Class II | 21 CFR 862.1155<br>Human chorionic gonadotropin test system | Clinical Chemistry (75) |

**H. Intended Use:**

1. Intended use(s):

   See indication for use below

2. Indication(s) for use:

   The DiaSorin LIAISON® XL HCG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® XL Analyzer for the quantitative determination of total human chorionic gonadotropin (hCG and βhCG) in human serum for early detection of pregnancy. Total hCG is the measurement of intact and beta-hCG.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   For use on the LIAISON® XL Analyzer

## I. Device Description:

The LIAISON® XL HCG assay is an in vitro diagnostic device consisting of reagents provided in individual compartments within a plastic container called the Reagent Integral. Each Reagent Integral contains:

- Solid Phase – magnetic particles coated with mouse monoclonal antibody against hCG, Bovine Serum Albumin (BSA), 0.09% $NaN_3$
- Calibrator 1 – low level hCG antigen (human) in phosphate buffer, BSA, 0.09% $NaN_3$
- Calibrator 2 – high level hCG antigen (human) in phosphate buffer, BSA, 0.09% $NaN_3$
- Conjugate – Monoclonal antibody against hCG (human) labeled with isoluminol, BSA, 0.09% $NaN_3$
- Assay Buffer- phosphate buffer, BSA, 0.09% $NaN_3$
- Specimen Diluent - phosphate buffer, BSA; 0.09% $NaN_3$

All human source material used in the preparation of this product has been tested by an U.S. FDA approved method and found non-reactive for the presence of the antibody to Human Immunodeficiency Virus 1 and 2 (HIV 1/2), the Hepatitis B surface antigen (HBV), and the antibody to Hepatitis C (HCV).

## J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche ELECSYS® HCG +Beta Test

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

   K003178

3. Comparison with predicate:

| Similarities and Differences | | |
|---|---|---|
| Item | New Device<br>LIAISON® XL HCG<br>(k131037) | Predicate Device<br>Roche ELECSYS® HCG +Beta Test (k003178) |
| Intended Use | In-vitro assay for the quantitative determination of total human chorionic gonadotropin (hCG and βhCG) in human serum for early detection of pregnancy. | Same |
| Measured Analyte | Total hCG<br>(intact and beta-hCG) | Same |
| Measuring range | 1.5 – 10,000 mIU/mL | 0.100 – 10,000 mIU/mL |
| Test principle | Chemiluminescent Immunoassay | Electrochemiluminescent Immunoassay |
| Sample Matrix | Human serum | Human serum and plasma |
| Sample size | 30µL | 10µL |
| Sample Handling and Processing | Automated | Same |
| Calibration | Two-point calibrator verification of stored master curve. Included with the kit. | Two-point calibrator verification of stored master curve. Not included with the kit. |
| Traceability | 3rd WHO reference standard IS 75/537. | 3rd WHO reference standard IS 75/537. |

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

- CLSI Guideline EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods;
- CLSI Guideline EP6-A, Evaluation of Linearity of Quantitative Analytical Methods;
- CLSI Guideline EP7-A2, Interference Testing in Clinical Chemistry;
- CLSI Guideline EP9-A2-IR, Method Comparison and Bias Estimation Using Patient Samples;
- CLSI Guideline EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures;
- CLSI Guideline C28-A3, Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory.

## L. Test Principle:

The method for the quantitative determination of hCG is a sandwich chemiluminescence immunoassay. A specific mouse monoclonal antibody is coated on the magnetic particles (solid phase); another monoclonal antibody is linked to an isoluminol derivative (isoluminol-antibody conjugate). All assay steps and incubations are performed by the LIAISON® XL Analyzer.

During the first incubation, hCG present in calibrators, samples or controls binds to the solid phase monoclonal antibody. After a washing step in the second incubation, the antibody conjugate reacts with hCG already bound to the solid phase. The starter reagents are then added subsequently and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU, relative light units) and is directly related to hCG concentration present in calibrators, samples or controls.

## M. Performance Characteristics (if/when applicable):

1. Analytical performance:

*a. Precision/Reproducibility:*

Following CLSI document EP5-A2, the sponsor evaluated precision using 3 commercial controls and 6 frozen serum samples with concentrations spanning the measuring range of the assay. The samples were tested using two reagent lots, in two replicates per run, 2 runs per day for 20 days (N=160 measurements per sample). Results of between lot and total precision are summarized in the table below.

| Panel ID# | N | mean mIU/mL | Between Lot | | Total | |
|---|---|---|---|---|---|---|
| | | | SD | %CV | SD | %CV |
| QC1 | 160 | 6.4 | 0.02 | 0.3% | 0.68 | 10.7% |
| QC2 | 160 | 23.3 | 0.07 | 0.3% | 1.41 | 6.0% |
| QC3 | 160 | 175.1 | 2.31 | 1.3% | 6.04 | 3.5% |
| Sample 1 | 160 | 60.2 | 0.01 | 0.0% | 2.95 | 4.9% |
| Sample 2 | 160 | 25.5 | 0.31 | 1.2% | 1.60 | 6.3% |
| Sample 3 | 160 | 431.4 | 6.44 | 1.5% | 13.03 | 3.0% |
| Sample 4 | 160 | 893.2 | 15.85 | 1.8% | 28.97 | 3.2% |
| Sample 5 | 160 | 4169.0 | 72.01 | 1.7% | 153.66 | 3.7% |
| Sample 6 | 160 | 9607.6 | 29.89 | 0.3% | 298.61 | 3.2% |

*b. Linearity/assay reportable range:*

Linearity:

The sponsor performed linearity studies in accordance with CLSI EP6-A guidelines using two high sample pools which were diluted to span the measuring range of the assay. A total of 10 or 11 samples for each linearity sample set were tested in duplicates on the LIAISON® XL analyzer. Samples tested ranged from 0.44 to 10379.0 mIU/mL. The observed values were plotted against the expected values and linear regression analysis was performed. Both sample sets yielded similar linear

regressions. Representative results are shown below.

$$y = 1.016x - 0.145, R^2 = 0.983$$

The data support the claimed measuring range of this device, 1.5 to 10,000 mIU/mL for serum samples.

Recovery:

The sponsor conducted a recovery study using five levels of spiked samples, which were prepared by adding the targeting amount of WHO 3rd reference standard into five human sera and tested in duplicates using one lot of reagents on one instrument. The overall % recovery for each spiked level was determined and evaluated for acceptance. The results are tabulated below. Additional recovery information at low levels is shown in the LoQ study (see below).

| Spiked level (mIU/mL) | Overall %recovery |
|---|---|
| 5 | 91.8 |
| 25 | 105.9 |
| 500 | 94.9 |
| 5000 | 92.9 |
| 9000 | 96.9 |

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

Traceability:

The LIAISON® XL HCG Calibrators 1 and 2 are traceable to the WHO hCG 3rd International Standard.

Value assignment:
Concentrations of kit calibrators are assigned through an internal procedure. Master standards consisting of 12 different concentrations spanning the complete assay range are prepared from a stock material of human hCG purchased from a commercial source. The concentrations of master standards were assigned through parallel testing with WHO 3rd reference standard. The master standards are then used to assign values to the kit calibrators over several runs and the mean results are used to determine the target values. The protocols for value assignment and acceptance criteria were reviewed and found to be adequate.

Kit Calibrators have the following target values:
Level 1: 13.0 – 19.0 mIU/mL
Level 2: 3000.0 – 4000.0 mIU/mL

Stability:
Shelf life and open vial stability of the reagent kit (including calibrators) were performed by the sponsor. Reagent kits are stable until the expiration date shown on the product labeling when stored as instructed. Open reagent vials are stable for 4 weeks when stored on board or at 2-8°C. The protocols for stability and acceptance criteria were

reviewed and found to be adequate.

*d. Detection limit:*

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were determined in accordance with CLSI document EP17-A2. LoB study was performed by measuring 60 replicates of one blank sample on 2 analyzers with 2 reagent lots per analyzer. LoB was calculated to be 0.17 mIU/mL. LoD study was performed by measuring 4 low concentration serum samples in the range of LoB to 4xLoB values, tested on 2 analyzers over 3 days with 2 reagent lots. LoD was calculated to be 0.36 mIU/mL. LoQ study was performed by spiking six negative samples with the WHO 3rd reference standard which were then tested over three days using three reagent lots. The sponsor claimed that the LoQ is 1.5mIU/mL, and demonstrated that the % bias is 15.5% and %CV is 12.3% at LoQ level.

*e. Analytical specificity:*

Interference:

Following CLSI guidance document EP7-A2, interference studies were performed by spiking common potential interfering substances into two serum samples pools that contain 5-9 mIU/mL and 45-64 mIU/mL hCG, respectively. The reference sample (control) without interferent was spiked with the respective amount of solvent. The matched spiked and control samples containing each interferent were tested on the LIAISON® XL HCG assay using 7 replicates with 1 reagent lot. The sponsor defines non-significant interference as bias within 10% between the spiked and the control samples. Results of non- significant interference are summarized in the table below:

| **Substance** | **Highest Concentration Tested** |
|---|---|
| Triglycerides | 3000 mg/dL |
| Hemoglobin | 1000 mg/dL |
| Unconjugated bilirubin | 20 mg/dL |
| Conjugated bilirubin | 20 mg/dL |
| Albumin | 6 g/dL |
| Rheumatoid Factor | 194 IU/L |
| Luteinizing Hormone (LH) | 500 mIU/mL |
| Follicle-stimulating hormone (FSH) | 500 mIU/mL |
| Human Growth Hormone (hGH) | 100 ng/mL |
| TSH | 200 mIU/L |
| Acetaminophen | 20 mg/dL |
| Acetylsalicylic Acid | 20 mg/dL |
| Ascorbic Acid | 20 mg/dL |
| Atropine | 20 mg/dL |
| Caffeine | 20 mg/dL |
| EDTA | 80 mg/dL |
| Ethanol | 1% |
| Gentisic Acid | 20 mg/dL |
| Glucose | 2 g/dL |
| Salicylic Acid | 20 mg/dL |

Hook effect:
The possible high dose hook effect was evaluated using sample spiked with hCG antigen up to 14,500,000 mIU/mL. This spiked sample was then serially diluted and measured in triplicates. No evidence of high dose hook effect was observed in the study for hCG concentration up to 14,500,000 mIU/mL.

*f. Assay cut-off:*
Not Applicable

2. Comparison studies:
   *a. Method comparison with predicate device:*
   Following the CLSI EP9-A2 guidance document, the sponsor performed a method comparison study of the LIAISON® XL HCG assay versus the predicate device. A total of 172 serum samples were compared across methods, of which 163 samples were in the measuring range (from 1.6 mIU/mL to 8460 mIU/mL on the LIAISON® XL HCG assay). Singlicate results from the candidate device and mean of duplicate results from the predicate device were used for the linear regression analysis. Weighted Deming regression analysis resulted the following:

$$Y_{(\text{Candidate Device})} = 0.973X_{(\text{Predicate})} - 0.223;\ R^2 = 0.993.$$

   A bias analysis of candidate device vs. predicate performed on the 163 samples exhibited an average bias of 2.7% (95% CI: 1.1 to 4.3%).

   *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:
   The reference range study was performed according to CLSI Guideline C28-A3. Human serum samples from apparently healthy non-pregnant premenopausal and postmenopausal subjects were tested to determine the reference range for the LIAISON® XL HCG assay. The results are listed below:

In a study performed on 74 healthy, non-pregnant premenopausal women (< 50-year olds), 97.5% of the values obtained were below 1.54 mIU/mL hCG.

In a study performed on 70 healthy, postmenopausal women (≥ 50-year olds), 97.5% of the values obtained were below 6.67 mIU/mL hCG.

**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.