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

A. 510(k) Number: k033234

B. Analyte: HCG, TSH

C. Type of Test: Chemiluminescent quantitative assays, utilizing competition assays and immunometric assays

D. Applicant: Edward Levine, Ph.D.
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Director, Clinical Affairs
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E. Proprietary and Established Names: Proprietary name: IMMULITE 2500 Automated Immunoassay Analyzer; Established name – Random access chemiluminescent immunoassay analyzer

F. Regulatory Information:

1. Regulation section: 21 CFR 862.2160, 862.1155, 862.1690

2. Classification: Class II & Class I (IMMULITE 2500)

3. Product Code: DHA, JLW, JJE

4. Panel: 75

G. Intended Use:

1. Intended use(s): The DPC IMMULITE 2500 analyzer is an automated immunoassay system intended to assay the same broad range of analytes in patient samples as does the IMMULITE 2000. The intent of the systems is to impart the same automation to the same array of immunoassays in the same hospital and commercial laboratory settings as the IMMULITE 2000. The system is intended to produce safe and effective performance when used by medical laboratory personnel as is the predicate system, IMMULITE 2000.

2. Indication(s) for use: The DPC IMMULITE 2500 analyzer is an automated immunoassay system intended to assay the same broad range of analytes in patient samples as does the IMMULITE 2000. The intent of the systems is to impart the same automation to the same array of

immunoassays in the same hospital and commercial laboratory settings as the IMMULITE 2000. The system is intended to produce safe and effective performance when used by medical laboratory personnel as is the predicate system, IMMULITE 2000.

3. Special condition for use statement(s):

4. Special instrument Requirements: For use with IMMULITE 2500 immunoassay reagents.

H. Device Description: Both the IMMULITE 2500 Automated Immunoassay and the predicate IMMULITE 2000 employ an automated conveyor system to move beads, which are the solid support for the assay through the various processing steps of sample and reagent addition, incubation, substrate addition and photon counting. Each system uses ¼ inch polystyrene antibody coated beads and assay specific antibody or antigen labeled with alkaline Phosphatase. The chemiluminescent detection system is a phosphate ester stabilized dioxetane. Cleavage of the Phosphatase ester alkaline phosphatase results in the decomposition of the dioxetane and the emission of light. The photon emission is quantified by luminometer via photon counting and is proportional to the quantity of the analyte present.

I. Substantial Equivalence Information:

1. Predicate device name(s): IMMULITE 2000

2. Predicate K number(s): k970227

3. Comparison with predicate:

Similarities and Differences		
Item	**DPC IMMULITE 2500 Device**	**DPC IMMULITE 2000 Predicate**
Operating principle	Chemiluminescent photon generation and detection	Chemiluminescent photon generation and detection
Intended use	IN Vitro diagnostic measurement of analytes in patient samples	IN Vitro diagnostic measurement of analytes in patient samples
Light Source	Chemiluminescent	Chemiluminescent
Detector	Photomultiplier tube	Photomultiplier tube

Detector Maximum/Minimum	20 Million CPS/ 200 CPS	20 Million CPS/ 200 CPS
Attenuation	Programmable 100 fold via neutral density filter	Programmable 100 fold via neutral density filter
Spectral Response	350 – 500 nm (FWHM)	350 – 500 nm (FWHM)
Incubation Time	Fully random access	30, 60, 90 minutes
Integration Time	One second	One second
Temperature Control	Assays incubated and read at 37^{O}C	Assays incubated and read at 37^{O}C
Pipetting of specimen and reagents	Automated, Programmable volume range of 5 – 20ul	Automated, Programmable volume range of 5 – 20ul
Separation method	Washing and axial centrifugation	Washing and axial centrifugation
Display	Flat panel Display	Flat panel Display
Printout	External graphics printer	External graphics printer
Interface	Dual port ram	Dual port ram
Assay principle	¼" Antibody coated plastic bead solid support with liquid alkaline Phosphatase conjugated reagent.	¼" Antibody coated plastic bead solid support with liquid alkaline Phosphatase conjugated reagent.

J. Standard/Guidance Document Referenced (if applicable): FDA Guidance *Deciding When to Submit a 510(k) for a Change of an Existing Device"* FOD 935; NCCLS EP-5

K. Test Principle: Competition Assays and Immunometric Assays utilizing Chemiluminescence

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility: The patient or patient pool samples were evaluated by an accelerated format of the NCCLS EP-5 protocol; two replicates of each specimen run on each of four assays per day over a 10 day period. This format yields 80 data points, which will be analyzed according to the NCCLS EP-5 algorithm. The IMMULITE 2500 average CV for the total precision shall be no more than 2% higher than the corresponding IMMULITE 2000 CV. **HCG** – Average total interassay precision 6.7% C.V. Acceptable Criteria <= 7.22% C.V. **TSH** – Average total interassay precision 5.5% C.V. Acceptable criteria - <= 10.0%

b. Linearity/assay reportable range: At least three specimens at various concentrations covering the assay range are used. The specimens are analyzed neat (undiluted) and diluted 1:2, 1:4, and 1:8. Slope of the linear regression comparing the observed and the expected values for each sample is between 0.90 – 1.10. Regression slopes ranging from 0.99 – 1.07, acceptable 0.90 – 1.10 (HCG) ranging from 0.95 – 1.05, acceptable 0.90 – 1.10 (TSH)

c. Traceability (controls, calibrators, or method): The IMMULITE 2500 calibration method employs a stored master curve in conjunction with a 2 point adjustment procedure. Analyte concentration is determined by a stored master curve. This standard curve is generated by the manufacturer for each lot of reagents and is provided as a “master curve”. Adjustors are then used to correlate counts per second (CPS) of the customer’s instrument to the CPS of the Instrument used by the manufacturer to generate a master curve. Master curves for each lot of reagents are generated on a single instrument by running numerous replicates of each standard, using a set of standards spanning the range of the assay. The standard replicates are collected in multiple runs. Replicates of a low and high adjustor are included in every run. Since the relationship between the laboratory instrument and the master curve signals is a straight line, only two points are needed to determine the line. These two points are defined by Adjustors run on the master instrument and the CPS run on the customer instrument during an adjustment. The slope and intercept of this line is then calculated. The slope and intercept are then used to observe to transform the CPS for an unknown to the CPS that would be observed on the master instrument. The purpose of the first adjustment of a new kit lot is

to correlate the CPS of the customer instrument to the master instrument. Adjustment is then performed at variable increments depending upon the assay.

d. Detection limit: Using calibrator A (zero calibrator as a sample), each method comparison study contains 20 replicates of the zero calibrator. The data are analyzed to determine the value associated with the counts that are 2SDs away from the average counts of the zero calibrator replicates. If the analytical sensitivity calculated from the IMMULITE 2500 is no greater than 110% of the analytical sensitivity of the IMMULITE 2000, the IMMULITE 2500 analytical sensitivity will be accepted. HCG analytical sensitivity 1.0 mlU/mL, TSH 0.01 mlU/mL. Functional sensitivity for the TSH assay was not determined.

e. Analytical specificity: At least three specimens at various concentrations covering the assay range are utilized. The assays are evaluated for the effects of the presence of hemoglobin up to 500 mg/dL, conjugated and unconjugated bilirubin up to 20 mg/dL, and lipids up to 3000 mg/dL. Criteria are not established but rather effects, if present, are reported in the package insert as to the type of sample that is acceptable for analysis.

f. Assay cut-off: To determine the minimum detectable concentration (MDC), or analytical sensitivity, of the IMMULITE 2500 HCG and TSH assay, 20 samples of the zero dose calibrator for each analyte was assayed in a single separate run for each analyte. Mean and standard deviations were calculated from the counts per second (CPS) for the 20 replicates. The apparent concentrations were determined at increasing standard deviations from the mean. The analytical sensitivity, defined as the concentration corresponding to two standard deviations above the average signal response of a sample free of the respective hormones, TSH and HCG, was assessed on five different runs and found to be – HCG 0.851, 0.628, 0.147, 0.782, and 0.588 mIU/mL, TSH – 0.011, 0.009, 0.009. 0.006 and 0.009 uIU/mL, on the IMMULITE 2500. Based on these studies the analytical sensitivity for the IMMULITE 2500 HCG is 1.0 mIU/mL and 0.01 mIU/mL for TSH. Functional sensitivity for the TSH assay was not determined.

2. <u>Comparison studies:</u>

a. Method comparison with predicate device: Comparisons were performed with 100 specimens covering the calibration range. Specimens on both the IMMULITE 2500 and the IMMULITE 2000 platforms. Controls and calibrators as well as patient samples are

run as unknowns; data are analyzed by linear regression. QC specifications for the IMMULITE 2000 lot to lot comparison for a specific assay will form the basis of the acceptance criteria for the linear regression comparison between the device and the predicate.

b. Matrix comparison: The HCG assay was compared to DPC IMMULITE 2000 on 145 patient serum samples and compared to the IMMULITE 2500 via linear regression: (IML2500) = (1.07x IML2000 + 11.6mIU/mL, r=0.993. Urine samples – a total of 123 urine samples from pregnant women were processed by the IMMULITE 2000 and by DPC's Double Antibody HCG. The samples, some of which were diluted, had HCG values ranging up to approximately 300 mIU/mL with a linear regression of IML2000 = 1.04x Dab -10mIU/mL, r=0.988.
The TSH assay was compared to the IMMULITE 2000 Rapid TSH on 100 serum samples with a concentration range to approximately 60 uIU/mL and was determined comparable with a linear regression of (IML 2500) =1.03(IML 2000) -0.01 uIU/mL, r=0.997

3. Clinical studies:
   a. *Clinical sensitivity:* N/A

   b. *Clinical specificity:* N/A

   c. *Other clinical supportive data (when a and b are not applicable):* N/A

4. Clinical cut-off: N/A

5. Expected values/Reference range: HCG – males and non pregnant females, 95% of the males measured below the assay detection limit of 1.1 mIU/mL and all were below 2.5 mIU/mL. Non pregnant females were 83% below detection limit 95% were below 2.5 mIU/mL and all were below 5.3 mIU/mL. A total of 593 serum samples from apparently healthy women were processed by the IMMULITE 2500 HCG Assay and are summarized in the product labeling. Urine – a result of greater than or equal to 30 mIU/mL is considered positive. A result less than 30 mIU/mL is considered negative.

   TSH – Based on its relationship with the IMMULITE 2000, the TSH 2500 assay can be expected to have essentially the same reference ranges. Euthyroid: 0.4 – 4.0 uIU/mL and Hyperthyroid: <0.01 uIU/mL

M. Instrument Name: Diagnostics Products Corporation IMMULITE 2500

N. System Descriptions:

1. Modes of Operation: Routine random analyzer

2. Software: The IMMULITE 2500 utilizes a PC based interface to the user with a color matrix display and a barcode reader for input and display of data.
3. FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes ___X_____ or No _____

4. Sample Identification: Bar code, computer based or user input

4. Specimen Sampling and Handling: samples vary depending upon assay. TSH - serum samples, HCG – serum samples, qualitative urine samples - urine

5. Assay Types: Competition assay or Immunometric (sandwich) assays

6. Reaction Types: Chemiluminescent

7. Calibration: The IMMULITE 2500 calibration method employs a stored master curve in conjunction with a 2 point adjustment procedure. Analyte concentration is determined by a stored master curve. This standard curve is generated by the manufacturer for each lot of reagents and is provided as a "mater curve". Adjustors are then used to correlate counts per second (CPS) of the customer's instrument to the CPS of the Instrument used by the manufacturer to generate a master curve. Master curves for each lot of reagents are generated on a single instrument by running numerous replicates of each standard, using a set of standards spanning the range of the assay. The standard replicates are collected in multiple runs. Replicates of a low and high adjustor are included in every run. Since the relationship between the laboratory instrument and the master curve signals is a straight line, only two points are needed to determine the line. These two points are defined by Adjustors run on the master instrument and the CPS run on the customer instrument during an adjustment. The slope and intercept of this line is then calculated. The slope and intercept are then used to observe to transform the CPS for an unknown to the CPS that would be observed on the master instrument. The purpose of the first adjustment of a new kit lot is to correlate the CPS of the customer instrument to the master instrument. Adjustment is then performed at variable increments depending upon the assay.

8. Quality Control: Use two controls low and high of HCG and TSH controls

O. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of The SE Determination Decision Summary.

P. Conclusion: Based upon the information provided, I recommend that the IMMULITE 2500 Analyzer and the assays for HCG and TSH be found substantially equivalent to the respective predicate devices.