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

A. 510(k) Number:

k182521

B. Purpose for Submission:

New device

C. Measurand:

Sex Hormone Binding Globulin (SHBG)

D. Type of Test:

Quantitative Immunoassay

E. Applicant:

Qualigen, Inc.

F. Proprietary and Established Names:

FastPack® IP Sex Hormone Binding Globulin Immunoassay

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1680 - Testosterone test system

2. Classification:

   Class I, reserved

3. Product code:

   CDZ

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indication(s) for use below.

2. Indication(s) for use:

   FastPack® IP SHBG is a chemiluminescent immunoassay intended for the quantitative determination of Sex Hormone Binding Globulin in human serum and plasma on the FastPack® System. The FastPack® IP SHBG assay is intended for use as an aid in the diagnosis of androgen disorders.

3. Special conditions for use statement(s):

   - For prescription use only.
   - Not for point-of-care use.

4. Special instrument requirements:

   FastPack® Analyzer

I. Device Description:

The FastPack® IP Sex Hormone Binding Globulin Immunoassay is dependent on a disposable reagent pack, the FastPack® Analyzer, calibrators, and controls.

Each FastPack® IP Sex Hormone Binding Globulin Reagent Pack contains:

- Paramagnetic Particles coated with streptavidin-monoclonal anti-SHBG antibody linked to covalently biotin, 150 µL
- Monoclonal anti-SHBG antibody covalently linked to alkaline phosphatase and Monoclonal anti-SHBG antibody covalently linked to biotin, 100 µL
- Wash Buffer, 2.0 mL
  Tris buffer containing surfactants
- Substrate, 145 µL
  ImmuGlow™ Plus: Indoxyl-3-phosphate and lucigenin in buffer containing preservatives

Each FastPack® IP Sex Hormone Binding Globulin Immunoassay Kit contains:

- 60 FastPack® IP Sex Hormone Binding Globulin Reagent Packs
- 64 Sample diluent vials, 0.9 mL each
- 1 Vial FastPack® SHBG Calibrator, 2.0 mL
- 1 Vials FastPack® SHBG Control 1, 2.0 mL
- 1 Vials FastPack® SHBG Control 2, 2.0 mL
- 1 Calibration Card
- 1 Control Range Card

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Beckman Coulter Access Sex Hormone Binding Globulin Reagent

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

   k083867

3. Comparison with predicate:

Similarities		
Item	**Candidate Device** FastPack® IP Sex Hormone Binding Globulin Immunoassay (k182521)	**Predicate Device** Access Sex Hormone Binding Globulin Reagent (k083867)
Intended Use/ Indications for Use	For the quantitative determination of sex hormone binding globulin in human serum and plasma.	Same
Assay format	Paramagnetic particle, chemiluminescent, two-site sandwich immunoassay employing specific monoclonal antibodies	Same
Assay procedure	Automated	Same
Components	Mouse monoclonal antibody against SHBG in the capture phase and a mouse monoclonal anti-SHBG antibody conjugated to alkaline phosphatase in the signal phase.	Same
Sample type	Serum or lithium-heparin plasma	Same
Testing Environment	Professional use	Same

Differences		
Item	**Candidate Device** FastPack® IP Sex Hormone Binding Globulin Immunoassay (k182521)	**Predicate Device** Access Sex Hormone Binding Globulin Reagent (k083867)
Claimed measuring range	0.8-174 nmol/L	0.33-220 nmol/L

Differences		
Item	**Candidate Device** FastPack® IP Sex Hormone Binding Globulin Immunoassay (k182521)	**Predicate Device** Access Sex Hormone Binding Globulin Reagent (k083867)
Expected Values/Reference Intervals	Males (18-50 years): 8.4-64.3 nmol/L Males (≥ 50 years): 8.8-107.4 nmol/L Females (12-46 years): 8.7-126.6 nmol/L Females (> 46 years): 8.9-131.1 nmol/L	Males (20-50 years): 13.3-89.5 nmol/L Females (20-46 years): 18.2-135.5 nmol/L Females (47-91 years): 16.8-125.2 nmol/L
Approximate assay time	8 minutes	28 minutes
Traceability	Traceable to the WHO 082/266 reference material	Traceable to the WHO 95/560 reference material

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

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures

CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures

CLSI EP07-A2, Interference Testing in Clinical Chemistry and CLSI EP37, Supplemental Tables for Interference Testing in Clinical Chemistry

CLSI EP28-A3C, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory

L. Test Principle:

The FastPack® IP Sex Hormone Binding Globulin Immunoassay is a chemiluminescent paramagnetic particle, two-site sandwich immunoassay that employs specific monoclonal antibodies. A mixture of biotinylated anti-SHBG specific antibody and anti-SHBG antibody labeled with alkaline phosphatase reacts with SHBG from the patient's sample forming a sandwich complex in the mixture. Streptavidin-coated paramagnetic particles are added to the reaction mixture. Wash steps remove unbound materials. Chemiluminogenic substrate is added to the bound complex and the chemiluminescence signal (relative luminescence units) is measured. The amount of relative luminescence units is directly proportional to the concentration of SHBG in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility

Precision was evaluated following CLSI EP5-A3 guideline. Seven serum patient samples with concentrations range ~5 to ~150 nmol/L SHBG were tested in duplicate determinations in each of two runs per day on each of three reagent lots. Testing was performed over a period of 20 non-consecutive days to yield 80 replicate determinations for each sample.

The precision results from one representative lot are summarized in the table below:

Sample	Mean (nmol/L)	Within-Run		Between Run		Between Day		Total	
		SD	% CV	SD	% CV	SD	% CV	SD	% CV
1	5.02	4.88	4.88	0.0	0.0	0.16	3.20	0.29	5.83
2	16.74	0.74	4.40	0.89	5.29	0.88	5.24	1.45	8.65
3	29.97	1.58	5.27	1.97	6.56	0.37	1.25	2.55	8.51
4	63.53	2.99	4.71	3.36	5.29	2.57	4.04	5.18	8.15
5	94.47	7.31	7.74	5.33	5.64	4.44	4.70	10.07	10.66
6	107.81	8.31	7.70	4.59	4.26	8.03	7.44	12.43	11.53
7	150.43	4.16	4.16	0.0	0.0	4.28	2.85	7.58	5.04

b. Linearity/assay reportable range:

The linearity study was conducted following CLSI EP06-A guideline. A high serum sample pool with a value > 180 nmol/L SHBG was intermixed with a low serum sample pool to make 11 concentrations spanning the intended linear range of the assay. All samples were run in quadruplicate determinations versus one FastPack® reagent lot on one FastPack® analyzer. The following linearity regression equation was obtained:

$y=0.9861x + 0.4787$; $r^2 = 0.9993$

The results of this study demonstrate that this method is linear for a measuring range of 0.8 to 174 nmol/L.

c. Traceability

The FastPack® IP Sex Hormone Binding Globulin Immunoassay is traceable to the WHO 082/266 reference material.

d. Detection limit:

Detection capability studies were conducted per CLSI EP17-A2 guideline.

For the limit of blank (LoB) study a total of 180 replicate determinations of a blank sample were run over 4 days on 6 FastPack® analyzers using three lots of FastPack® reagents. Data was analyzed using the non-parametric approach per CLSI EP17-A2 guideline. Based on the results of the study, the LoB was set to 0.08 nmol/L.

The limit of detection (LoD) study was conducted by testing 4 low-level SHBG samples over 4 days on 6 FastPack® analyzers using three lots of FastPack® reagents. LoD was determined based on the lowest amount of analyte in a sample that can be detected with type I and II error rates set to 5% . Based on the results of the study, the LoD was set to 0.20 nmol/L.

The limit of quantitation (LoQ) study was conducted by testing 4 low-level samples over 4 days on 6 FastPack® analyzers using three lots of FastPack® reagents. The LoQ was defined as the lowest concentration wherein a <20% CV occurs. The LoQ was calculated for each lot of reagents, and the LoQ that met the acceptance criteria at the representative performance reagent combination was selected. Based on the analysis of the study results the LoQ is set at 0.80 nmol/L.

The sponsor's claimed measuring range is 0.8-174 nmol/L.

e. Analytical specificity:

Interference and cross-reactivity studies were conducted using two serum sample pools, one containing ~10 nmol/L SHBG and the second containing ~70 nmol/L SHBG were prepared. Aliquots of the samples were spiked with interfering endogenous and exogenous substances at varying concentrations and run against one lot of FastPack® reagents on seven FastPack® analyzers in triplicate determinations. The sponsor defines significant interference as ±10% bias compared to the control results. The results of the interference study are summarized in the table below:

Compound	Highest level demonstrating no interference
Conjugated Bilirubin	400 mg/mL
Unconjugated Bilirubin	300 mg/mL
Hemoglobin	10 g/L
Lipid	10 g/L
d-Biotin	2000 ng/mL

No cross-reactivity was detected for the following substances and concentrations:

Compound	Highest level demonstrating no cross-reaction or interference
Transferrin	0.5 g/dL
Heparin	10,000 U/dL
Low Molecular Weight Heparin (LMWH)	0.6 U/dL
Human Albumin	8.0 g/dL
Human IgG	1.0 g/dL
Thyroxine Binding Globulin (TBG)	20 mg/dL
Thyroglobulin	300 µg/L
Testosterone	2.5 mg/dL
Laminin	6,000 µg/L
GAS6	250 µg/L
Protein S	30 mg/L
Estradiol	4.0 mg/dL
11-deoxycortisol	0.5 mg/dL
5α-dihydrotestosterone	2.0 mg/dL
Cortisol	10 mg/dL
Alpha-fetoprotein (AFP)	500 µg/L
Ibuprofen	60 mg/dL
Acetaminophen	10 mg/dL
Acetylsalicylic Acid	80 mg/dL

HAMA interference*:*
For the human anti-mouse antibodies (HAMA) interference, two serum sample pools, one containing ~10 nmol/L SHBG and the second containing ~70 nmol/L SHBG were prepared. Aliquots of the samples were spiked with concentrations up to 4 µg/mL HAMA and run against one lot of FastPack® reagents on one FastPack® analyzer in triplicate determinations. In addition, six patient samples (3 HBV-3 HIV false positive samples which represent specimens with high levels of heterophilic antibodies) were spiked with either saline (as a control) or heterophilic blocking reagent to determine the effect of the heterophile activity in relation to the saline control. The sponsor defines significant interference as ±10% bias as compared to the control results. Based on the results of these studies, the FastPack® IP Sex Hormone Binding Globulin Immunoassay did not show HAMA interference up to 4 µg/mL or to the additional heterophile antibodies tested.

High-dose hook effect:
To evaluate the potential for high dose hook effect on the FastPack® IP Sex Hormone Binding Globulin Immunoassay, samples were prepare to generate SHBG concentrations values of 2500, 1000, and 400 nmol/L. Each sample was assayed in triplicate determinations against one FastPack® reagent lot on two FastPack® analyzers. The results demonstrate that the FastPack® IP Sex Hormone Binding Globulin Immunoassay displays no hook effect up to and including 1000 nmol/L SHBG.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed by testing a total of 158 human serum samples using the candidate device and the predicate device. The serum samples concentrations ranged between 5.7 to 176 nmol/L SHBG, as determined by the predicate device. The following results were obtained using Passing-Bablok analysis: r= 0.985, slope = 0.993 (95% CI: 0.967 to 1.019) , and y-intercept = -0.614 nmol/L (95%CI: -2.21 to 0.982) .

b. Matrix comparison:

A matrix comparison study was performed by testing 54 matched serum and lithium heparin plasma samples. The samples were tested in singlet determinations on each of two FastPack® Analyzers against one lot of FastPack® IP Sex Hormone Binding Globulin Reagents. Passing-Bablok regression was performed using the first replicate obtained from each matrix and the slope was 0.987, y-intercept = 0.992 nmol/L, r=0.987 (r^2 = 0.973).

The results of the matrix comparison study support the manufacturer's claim that serum and lithium heparin plasma are acceptable sample types to use with the FastPack® IP Sex Hormone Binding Globulin Immunoassay.

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:

A reference range study was performed by testing a total of 613 serum samples from apparently healthy individuals with no known pre-existing endocrine disorders. Samples were assayed in singlet determinations using three FastPack® IP Sex Hormone Binding Globulin Reagent Pack lots. Reference ranges were determined using non-parametric 2.5th – 97.5th percentiles (central 95%). The results of the reference range study are presented in the table below.

Table 3: FastPack® IP Sex Hormone Binding Globulin Immunoassay Reference I

Partition	N	Median (nmol/L)	Reference Interval (nmol/L)
Males 13 – 50 years	149	26.6	9.4 – 61.8
Males > 50 years	155	35.9	13.0 – 86.4
Females 12 – 46 years	151	39.6	9.2 – 134.4
Females > 46 years	158	49.8	12.2 – 121.2

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

O. Conclusion:

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