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510(k) Summary of Information Respecting Safety and Effectiveness

- A. Submitter:
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- B. Device Names:
Proprietary Name: Biocircuits IOS™ Serum Pregnancy Test Cartridges
Biocircuits IOS™ Immunoassay Controls
(formerly IOS™ Thyroid Controls)
- Common Names: Reagents for hCG (human chorionic gonadotropin)
Quality control materials (assayed and unassayed)
- Classification Name: human chorionic gonadotropin (hCG) test system
Quality control materials (assayed and unassayed)
- C. Legally Marketed Device:

The IOS Serum Pregnancy Test Cartridges are substantially equivalent to the Hybritech ICON II hCG ImmunoConcentration Assay currently manufactured and distributed by Hybritech Incorporated.

D. Device Description:

Serum Pregnancy Test Cartridges: Human chorionic gonadotropin is a glycoprotein that is synthesized by the placenta during pregnancy. hCG appears in both serum and urine relatively soon after implantation of the developing embryo. The presence of hCG, and its rapid rise following conception, is thus the basis of pregnancy testing. hCG testing can aid in the determination of ectopic pregnancy and spontaneous abortion. hCG is also secreted by a wide variety of tumors: gestational trophoblastic tumors, testicular and prostatic tumors, and some breast cancers.

hCG is composed of two noncovalently linked polypeptides: the alpha and beta subunits. The individual subunits lack biological activity, but become active when linked to form the intact hormone. The alpha subunit of hCG is structurally similar to the alpha subunits of LH (luteinizing hormone), FSH (follicle stimulating hormone), and TSH (thyroid stimulating hormone). The beta subunits of each of the hormones are structurally unique and confer the biologic and immunologic specificity to each hormone. The beta subunit of hCG contains a unique chain of 30 carboxy-terminal amino acids that confers its specificity (1). Monoclonal antibodies directed against this portion of the beta subunit permit differentiation between hCG and the other pituitary glycoprotein hormones.

Principle of the Test

The IOS™ Serum Pregnancy test is a two-site simultaneous sandwich immunoassay which utilizes two antibodies directed against intact hCG: a polyclonal antibody immobilized on the plastic cartridge surface (capture antibody) and a monoclonal antibody labeled with alkaline phosphatase (detection antibody, 'conjugate'). hCG in the patient sample binds to conjugate in the test cartridge, and this hCG-conjugate complex then binds to the immobilized capture antibody. After a short incubation period, excess hCG-conjugate complex is washed away. Substrate is added, which reacts with the alkaline phosphatase conjugate-hCG-capture antibody 'sandwich' and produces a fluorescent signal. The level of fluorescence is directly proportional to the amount of bound hCG-conjugate, which is directly proportional to the amount of hCG present in the patient sample. All reagents necessary to perform the test are dried in the IOS™ cartridge, and are rehydrated by the addition of patient sample by the operator, or by the addition of buffer by the instrument.

To perform a test, the operator inserts an IOS™ Serum Pregnancy Test Cartridge in the IOS™ instrument. When prompted, the operator adds sample to a sample well. Each cartridge can test two different patient samples, with one patient sample added to the left well and the second to the right well. The operator starts the test sequence when sample addition is complete. Patient sample rehydrates conjugate dried in the sample well; the conjugate binds to hCG present in the patient serum sample. This hCG-conjugate complex then flows into the incubation/reaction chamber where it binds to the immobilized capture antibody. At the end of the incubation time, excess sample-conjugate is washed away by buffer. Buffer is used to rehydrate the dried substrate necessary for signal generation and quantitation of hCG, in a second reaction chamber. Substrate flows into the incubation/reaction chamber where signal is produced as a result of substrate reacting with conjugate bound to captured patient hCG (the 'sandwich'). The fluorescent signal is read as a rate by front-surface fluorometry, compared to the rate for the cut-off value stored in the barcode on the test cartridge, and determined to be higher or lower than the cut-off value.

Immunoassay Controls: The use of materials derived from human blood to monitor quality control of clinical chemistry testing in the clinical laboratory has been widely established over the past several years. The Biocircuits IOS™ Immunoassay Controls are two levels of blood-based material for use with Biocircuits IOS™ Test Cartridges.

To run a control, the operator inserts the Control Cartridge (packaged with the controls) into the IOS™ instrument. The instrument reads the lot number and ranges of acceptable values for the control solutions from the Control Cartridge barcode, and then ejects the Control Cartridge. The operator then inserts a test cartridge and follows the instrument prompts to identify the control level, apply control solutions, and begin the test sequence. The IOS™ instrument performs the required buffer additions to rehydrate assay reagents and perform wash steps as necessary, reads the fluorescence signal generated, and calculates and prints the control result just as it would if the cartridge were used to test a patient sample.

E. Intended Use:

The IOS™ Serum Pregnancy Test Cartridge is to be used for the qualitative determination of human chorionic gonadotropin (hCG) in serum for the early detection of pregnancy. It is intended to be used with the IOS™ instrument in clinical laboratories, physicians' office laboratories, and other alternate sites of use close to the point of patient care.

The IOS™ Immunoassay Controls Kit is to be used to assist in monitoring accuracy and precision in the IOS™ immunoassay test cartridges.

F. Comparison with the Predicate Device:

Table I summarizes the comparative features of the IOS and Hybritech assays.

G. Performance Data:

1. Serum Pregnancy Test Cartridges:

Non-clinical testing performed in the manufacturer's laboratories gave the following results:

Sensitivity (Detection Limit or Cut-off Value)

The analytical sensitivity of the IOS™ Serum Pregnancy Test is defined as the detection limit, or cut-off value, of the assay. Sixty replicates of a zero calibrator were run using IOS™ Serum Pregnancy Test Cartridges. The mean value and standard deviation of the signal were calculated. The sensitivity was obtained by interpolating two standard deviations above the mean signal of the zero calibrator. The analytical sensitivity of the IOS™ Serum Pregnancy Test is 25 mIU/mL.

The cut-off value was confirmed by spiking serum samples from normal males with different levels of hCG below, at, and above the cut-off value. Samples containing 0, 15, 20, 25, 30, 35, 40 and 100 mIU/mL hCG were tested in IOS™ Serum Pregnancy Test Cartridges. The IOS™ Serum Pregnancy Test Cartridges gave positive results in 100% of the samples containing 25 mIU/mL hCG; all samples containing > 25 mIU/mL hCG also tested 100% positive.

Accuracy (Correlation)

Serum samples were tested using the IOS Serum Pregnancy Test and the Hybritech ICON II HCG ImmunoConcentration™ Assay, a qualitative test for serum hCG. Results obtained using the IOS Serum Pregnancy Test agreed with the ICON II Assay in 142 (100 %) of the positive samples tested (n = 142). The IOS Serum Pregnancy Test agreed with the ICON II Assay in 146 (98 %) of the negative samples tested (n = 149).

Cross-Reactivity

Potential cross-reacting substances were added to serum samples containing 0 and 100 mIU/mL hCG at the levels specified below, and tested in the IOS Serum Pregnancy Test. None of the substances interfered with the test results.

LH at 500 mIU/mL
FSH at 500 mIU/mL
TSH at 500 uIU/mL

Interfering Substances

Potential interfering substances were added to serum samples containing 0 and 100 mIU/mL hCG at the levels specified below, and tested in the IOS Serum Pregnancy Test. None of the substances interfered with the test results.

Hemoglobin at 500 mg/dL
Bilirubin (unconjugated) at 20 mg/dL
Cholesterol at 750 mg/dL
Triglycerides at 750 mg/dL

Clinical testing performed in three typical physicians' office laboratories gave the following results:

Samples were tested by users in three typical physicians' office laboratories. Sites of testing included an OB/GYN practice, an Internal Medicine practice, and a Reproductive Endocrinology/Fertility practice. Users included medical technologists, medical assistants, and front-office personnel. A total of 172 patient samples were tested using the IOS™ Serum Pregnancy Test cartridges in the office laboratories; samples tested included those from pregnant females, non-pregnant females, post-menopausal females, and males. The samples were tested in the manufacturer's laboratory using the ICON II assays. Results obtained using the IOS Serum Pregnancy Test agreed with the ICON II Assay in 81 of 82 (98.7%) of the positive samples tested and in 90 of 90 (100%) of the negative samples tested.

2. Immunoassay Controls

The following ranges for the IOS™ Immunoassay Controls were determined in studies in the manufacturer's laboratories. To establish the ranges, the controls were tested in at least 40 cartridges each, over at least 10 days, using several IOS™ instruments. These values only apply to this lot of IOS™ Immunoassay Controls. Different lots of Immunoassay Controls will likely have slightly different ranges. Your laboratory should establish its own range for these controls over time.

Analyte	Control Level 1		Control Level 2	
	Mean	Range	Mean	Range
T4 (ug/dL)	8.1	6.48-9.72	12.9	10.32-15.4
T-Uptake (%)	32.4	29.25-35.55	39.7	36.85-42.55
Serum Preg. Test	Negative		Positive	

It is self-evident from the data and information presented here that the Biocircuits IOS™ Serum Pregnancy Test Cartridges are as safe, effective, and perform as well as the Hybritech ICON II hCG Immunoconcentration Assay manufactured and distributed by Hybritech Incorporated.

Attachment: Table I: Assay Comparison

TABLE 1
Hybritech ICON II vs. Biocircuits IOS™
Assay Comparison

ATTRIBUTE	Hybritech ICON II hCG	IOS™ Serum Pregnancy Test
Technology	Immunoconcentration immunoassay	Fluorometric enzyme immunoassay
Assay format	Sandwich	Sandwich
Enzyme label	Alkaline phosphatase	Alkaline phosphatase
Substrate	Bromochloroindolyl phosphate (BCIP)	4-Methylumbelliferyl phosphate (4-MUP)
Reagents		
Immobilization Medium	Paper membrane	Plastic cartridge
Dry reagents	Monoclonal antibody only	Monoclonal antibody, polyclonal antibody conjugate, substrate
Wet reagents	3 (for urine) or 4 (for serum), each added by operator as needed	1 (for all assays), always on board, added by instrument as needed
Delivery of wet reagents	Manual, dropwise	Fully automated, precisely measured
Stability	Three months at room temperature	Four months at room temperature
Storage	Room Temperature (15-30°C) or Refrigerated (2-8°C)	Room Temperature (15-30°C)
Sample		
Type	Serum or urine	Serum
Volume	450 uL (serum) 250 uL (urine)	33 uL
Preparation	Serum diluted by operator in separate container before addition to icon	None; serum diluted by instrument after addition to cartridge
Test Performance		
Hands-on Time	5+ minutes	Approximately one minute
Number of Steps	6, including serum dilution	One (sample addition to cartridge)
Test Result	Qualitative color development	Displayed on screen Printed alphanumeric hard copy
Test Interpretation	By operator Visual comparison to Positive Reference Zone and to Negative Control Zone	By instrument Comparison to cut-off value in software

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