

K9-3837

510(k) Summary of Information Respecting Safety and Effectiveness

A. Submitter:

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B. Device Names:

Proprietary Name: **Biocircuits IOS™ T4 Test Cartridge**
Biocircuits IOS™ Thyroid Controls

Common Names: Reagents for total thyroxine assay
Quality control material (assayed and unassayed)

Classification Name: Total thyroxine test system

c. Legally Marketed Device:

The IOS™ T4 Test Cartridges are substantially equivalent to the Stratus T4 test currently in commercial distribution by Dade International.

D. Device Description:

Thyroxine (T4) is a hormone that is synthesized and stored in the thyroid gland, plays a vital role in growth and maturation, and is essential in the control of metabolism in all bodily organs. More than 99% of T4 is reversibly bound to three plasma proteins in the blood: thyroxine-binding globulin (TBG), thyroxine-binding prealbumin (TBPA), and albumin. The balance of T4 is in the free, unbound state in blood at any one time.

Malfunction of the thyroid gland may result in abnormal concentrations of T4. Increased levels of T4 have been found in hyperthyroidism due to Grave's disease, toxic multinodular goiter, and in acute and subacute thyroiditis. Low levels of T4 have been associated with congenital hypothyroidism, myxedema, chronic thyroiditis (Hashimoto's disease), and with some genetic abnormalities.

Principle of the Test:

T4 Test: The IOS™ T4 test is a competitive immunoassay in which T4 in the sample is first released from the carrier proteins by 8-anilino-1-naphthalene sulphonic acid (ANS) and salicylate, and then competes with alkaline phosphatase-labeled T4 (conjugate) for binding sites on immobilized monoclonal anti-T4 antibody. After a short incubation, excess sample and conjugate are washed away. Substrate is added, which reacts with the alkaline phosphatase conjugate bound to antibody. The product of the enzyme-substrate reaction produces a fluorescent signal. The level of fluorescence is directly proportional to the amount of conjugate bound to the surface, and inversely proportional to the amount of T4 present in the patient sample. All reagents necessary to perform the test are dried in the IOS™ cartridge, and are dehydrated by the addition of patient sample by the operator, or by the addition of buffer by the instrument.

Thyroid 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™** Thyroid Controls are two levels of blood-based material for use with **Biocircuits IOS™** thyroid assay test cartridges.

To run a control, the operator inserts the Thyroid 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 T4 or T4/TU 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 **Biocircuits IOS™** T4 cartridge is to be used for the quantitative determination of total thyroxine levels, as part of the **Biocircuits IOS™** System.

The **IOS™** Thyroid Controls Kit is to be used to assist in monitoring accuracy and precision in the **IOS™** thyroid assays.

F. Comparison with the Predicate Device:

Table I summarizes the comparative features of both the **IOS™** and Stratus T4 assays.

G. Performance Data:

1. T4 Test Cartridges:

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

Sensitivity: The analytical sensitivity of the **IOS™** T4 assay is defined as the smallest concentration of T4 that can be distinguished from zero. Ten replicates of a zero calibrator were run using **IOS™** T4 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 sensitivity of the **IOS™** T4 assay is 1.85 ug/dL.

Specificity: Cross-Reactivity

The specificity of the monoclonal antibody used in the **IOS™** T4 assay was determined by evaluating the cross-reactivity with substances similar in structure to T4 or those known to interfere with the immunological reaction. Results are listed below. Pooled human serum with a value of 8.5 ug/dL T4 was used.

Compound	Cross-Reactivity
D-thyroxine (D-T4)	100%
L-triiodothyronine (L-T3)	<470
D-triiodothyronine (D-T3)	<2%
5-diiiodothyronine	<0.1%
5-diiiodotyrosine	<0.170
Phenytoin (diphenylhydantoin), at 10,000 ug/dL	<0.1%
Propylthiouracil, at 10,000 ug/dL	<0.170
Phenylbutazone, at 10,000 ug/dL	<0.1%
Salicylic acid, at 50 mg/dL	<0.170
Acetylsalicylic acid (ASA), at 50 mg/dL	<0.170

Specificity ~ Interfering Substances

The following substances were tested at the levels specified and found not to significantly affect the T4 result obtained using the IOS™ T4 cartridge. A pool of human serum with a value of 5.8 ug/dL T4 was used.

Substance	Interference
Hemoglobin @ 500 mg/dL	6%
Bilirubin (unconjugated) @ 20 mg/dL	6%
Cholesterol @ 500 mg/dL	1%
Triglycerides @ 750 mg/dL	4%

Precision: The following results were obtained from a laboratory study performed at the manufacturer for within-day, between-day, and total imprecision:

Control Level	1	2	3
Mean (ug/dL T4)	8.1	12.9	47.65
SD, overall (ug/dL)	0.72	1.14	0.56
% CV, within-day (n=10)	8.5%	8.8%	14.4%
% CV, between-day (n=40)	5.0%	4.4%	6.9%
% CV, total	8.9%	8.8%	12.1%

Accuracy: Spiked Recovery

A normal human serum pool with a known T4 value was spiked with different quantities of T4 and then assayed in duplicate using IOS™ T4 cartridges. The results are as shown:

Endogenous [T4] (ug/dL)	Added [T4] (ug/dL)	Average Observed (ug/dL)	Average Recovery (%)
4.25	3.5	7.55	93%
4.25	6.0	10.2	99%
4.25	9.2	13.5	100%
4.25	12.4	16.5	99%
4.25	18.0	20.7	91%

Accuracy: Correlation

A comparison of methods obtained by testing 126 patient samples in the manufacturer's laboratories using the IOS™ T4 cartridges and a commercially available fluorescent enzyme immunoassay gave a correlation coefficient (r) of 0.937, **with the line of linear regression described by the equation $y = 0.29 + 0.943x$** . The samples tested ranged from 1.8 ug/dL to 24.6 ug/dL T4.

Clinical testing performed at a typical physicians office laboratory gave the following results:

Precision:

Control Level	1	2	3
number of replicates	22	24	22
Mean (ug/dL T4)	7.46	11.75	4.79
SD, overall (ug/dL)	0.75	1.40	1.01
% CV, total	10.1%	11.9%	21.2%

Accuracy: Correlation

A comparison of methods was performed by users in a typical physicians' office laboratory. A total of 43 patient samples were tested using the IOS™ T4 cartridges in the office laboratory; the samples were split and sent to the manufacturer's laboratory for retesting on both the IOS™ and on the predicate device. These studies gave a correlation coefficient (r) of 0.919 with the predicate device, **with the line of regression described by the equation $y = 1.915 + 0.771x$** . The samples tested ranged from 1.8 ug/dL to 20.6 ug/dL T4.

Expected Values:

In a Preference range study of 125 normal, healthy adults (98 males and 27 females) in the manufacturer's laboratories, the range of T4 values for the IOS™ T4 assay was determined to be 4.6 - 11.3 ug/dL.

T4 levels are generally depressed in hypothyroid patients and generally elevated in hyperthyroid patients. T4 levels may also be elevated in neonates and infants.

Since T4 values may vary with many factors, such as geographic location, local population, diet, etc., these ranges are provided for general informational purposes and may not apply to your specific patient population. We recommend that each laboratory establish its own reference ranges for its patient population.

2. Thyroid Controls

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

<u>Control</u>	<u>T4 (ug/dL)</u>		<u>T-Uptake (%)</u>	
	Mean	Range	Mean	Range
1	8.1	6.48-9.72	32.4	29.25-35.55
2	12.9	10.32-15.48	39.7	36.85-42.55

It is self-evident from the data and information presented here that the Biocircuits IOS™ T4 Test Cartridges are as safe, as effective, and perform as well as the Stratus T4 assay in commercial distribution by Dade International.

Attachment: Table I: Assay Comparison

TABLE 1
Baxter STRATUS vs. Biocircuits IOS™
Assay Comparison

<u>ATTRIBUTE</u>	<u>STRATUS T4</u>	<u>IOS T4</u>
Technology	Radial partition immunoassay	Plastic cartridge, competitive immunoassay
Assay format	Sequential	Competitive
Enzyme label	Alkaline phosphatase	Alkaline phosphatase
Substrate	Methylumbelliferyl phosphate	Methylumbelliferyl phosphate
Reagents Immobilization Medium Dry	Reaction tab Monoclonal antibody only	Plastic cartridge Monoclonal antibody, ANS, T4-AP, substrate
Wet Delivery Calibration Calibration Stability Storage	3, loaded by operator at start of each run Fully automated User-generated 14 days (minimum) Refrigerated (2-8°C)	1, continuously on board Fully automated Factory-generated 60 days minimum Room Temperature (15-30°C)
Sample Type Volume Dilution	Serum or plasma 0.2 ml (minimum) Performed by instrument	Serum 0.033 ml Performed by instrument
Operating environment	22°-320 C	15°-300 c
Data analysis	Microprocessor-controlled Stored standard curves	Microprocessor-controlled Stored standard curves
Data output	LCD display Printed alphanumeric hard copy	LCD display Printed alphanumeric hard copy