OCT 13 1998

BIOCIRCUITS corporation 1324 Chesapeake Terrace, Sunnyvale, California 94089

510(k) Summary
IOS PSA Test Cartridges

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K981634

A. Submitter:

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Contact: Sheila Ramerman
Date Prepared: May 7, 1998

B. Device Names:

Proprietary Name: Biocircuits IOS® Prostate Specific Antigen Test Cartridges
Biocircuits IOS® PSA Controls

Common names: Fluorometric enzyme immunoassay for prostate specific antigen
Quality control materials (assayed and unassayed)

Classification Name: Prostate Specific Antigen Test System
Quality control materials (assayed and unassayed)

C. Legally Marketed Device:

The IOS Prostate Specific Antigen Test Cartridges are substantially equivalent to the Hybritech Tandem-E® PSA ImmunoEnzyMetric Assay, currently manufactured and distributed by Hybritech Incorporated.

D. Device Description:

Prostate Specific Antigen Test Cartridges:

Prostate specific antigen (PSA) is a serine protease first discovered in seminal plasma which has a molecular weight of approximately 30,000 Daltons.[1,2] PSA is secreted by normal prostatic epithelial cells as well as by diseased prostatic tissue.[3] When PSA is released into the blood, it is inactivated by the major extracellular serine protease inhibitors, alpha-2-macroglobulin and alpha-1-antichymotrypsin. The portion of PSA that is inactivated by alpha-2-macroglobulin is undetectable by immunoassays measuring total PSA.[4-6] The fraction of PSA bound to alpha-1-antichymotrypsin (~90 kDa) is detectable and is the predominate form of PSA in human serum, constituting 73 -95% of

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circulating PSA. The remaining 5 - 27% of detectable PSA exists in a "free" enzymatically inactive state (~30 kDa), and is found to be at higher proportions in patients with benign prostatic hyperplasia.[7] The IOS PSA assay measures free and total PSA in an equimolar fashion.

Longitudinal determinations of PSA have been shown to be useful when monitoring prostate cancer patients. Serial PSA measurements are indicative of recurrence of disease or metastatic progression if PSA levels continue to rise after surgical or medical treatment. Serial PSA measurements that decrease to undetectable levels indicate successful treatment of disease.[8-11]

PSA levels have also been shown to be elevated in patients with benign prostatic hyperplasia (BPH) and prostatitis.[10] PSA levels are not elevated in cancers of the breast, lung, colon, rectum, stomach, pancreas, or thyroid.

PSA testing alone is not be used as a screening test for prostate cancer or in the staging of prostatic cancer. PSA testing is accepted as an adjunctive test in managing the treatment of patients with prostate cancer.[12,13]

Principle of the Test

The IOS PSA test is a two-site sandwich immunoassay. PSA in the patient serum binds to an enzyme-labeled monoclonal anti-PSA conjugate. This PSA:conjugate complex is captured by polyclonal anti-PSA antibody immobilized on the plastic surface, forming a capture-antigen-conjugate sandwich. After an incubation period, excess sample and conjugate are washed away and substrate is added. The substrate reacts with the conjugate:PSA complex captured on the surface and produces a fluorescent signal. The rate of the enzyme-substrate reaction is directly proportional to the amount of conjugate bound, which is directly proportional to the amount of PSA present in the patient sample. All reagents necessary to perform the test are dried on the IOS test cartridge, and are rehydrated by the addition of patient sample, or by the addition of IOS buffer by the instrument.

To perform the test, the operator inserts an IOS PSA cartridge into the IOS instrument. When prompted, the operator adds sample to the sample well and starts the test sequence. The instrument draws the cartridge inside to mix the patient sample, which also rehydrates the anti-PSA conjugate. A short incubation period allows the serum and conjugate to react. The PSA:conjugate complex then flows into the incubation/reaction chamber where binding to the solid phase occurs. At the end of this incubation time, excess patient sample and conjugate are aspirated out of the incubation/reaction chamber and the incubation/reaction chamber is washed using buffer added by the instrument. Buffer is also used to rehydrate the substrate necessary for signal generation and quantitation of PSA in another reagent chamber; rehydrated substrate is then allowed to enter the incubation/reaction chamber. The fluorescent signal produced is read as a rate by front-surface fluorometry, compared to the rates produced by a series of calibrators stored in the instrument memory, and the amount of PSA present in the patient sample is calculated from the stored calibration curve.

IOS PSA 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 PSA Controls are two levels of blood-based material for use with Biocircuits IOS PSA 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 Prostate Specific Antigen Test Cartridges are to be used for the quantitative determination of prostate specific antigen levels in serum as an aid in the management of patients diagnosed with prostate cancer. They are 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 PSA Controls are to be used to assist in monitoring accuracy and precision in the IOS PSA Test Cartridges.

F. Comparison with the Predicate Device:

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

G. Performance Data:

Prostate Specific Antigen Test Cartridges:

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

1. Precision:

Control Level	**1**	**2**	**3**
Mean (ng/mL)	2.6	10.1	23.3
SD, overall (ng/mL)	0.26	1.25	2.26
% CV, within-day (n=10)	11.3%	5.5%	7.6%
% CV, between-day (n=10 days)	10.0%	12.8%	8.6%
% CV, overall	10.2%	12.4%	9.7%

2. Accuracy:

A comparison of methods obtained by testing 319 patient samples in the manufacturer's laboratories using the IOS Prostate Specific Antigen assay and a commercially available enzyme immunoassay gave a correlation coefficient ('r') of 0.9924, with the line of regression described by the equation $y = 0.99*x + 0.35$ Samples tested ranged from 0.2 to 95.8 ng/mL.

TABLE 1
Hybritech Tandem-E® vs. Biocircuits IOS®
Assay Comparison

ATTRIBUTE	Hybritech (Manual method)	IOS
Technology	Colorimetric enzyme immunoassay	Fluorometric enzyme immunoassay
Assay format	Two-site sandwich	Two-site sandwich
Enzyme label	Alkaline phosphatase	Alkaline phosphatase
Substrate	p-Nitrophenyl phosphate	Methylumbelliferyl phosphate
Reagents		
Immobilization Medium	Plastic bead	Plastic cartridge
Dry	Monoclonal anti-PSA	Polyclonal anti-PSA, monoclonal anti-PSA conjugate, substrate
Wet	4, added manually by the operator	1 (diluent, used for all assays), continuously on board
Delivery	Manual	Fully automated
Calibration	User-generated	Factory-generated
Calibration Stability	Calibrators tested in each run	90 days (minimum)
Storage	Refrigerated (2-8°C)	Room Temperature (15-30°C)
Sample		
Type	Serum	Serum
Volume	0.1 ml	0.130 mL
Measurement Needed	Precision	Precision
Operating environment	18° - 25° C	15°-30° C
Data analysis	Computer-assisted, indepent of photometer User-generated standard curves	Microprocessor-controlled, in instrument Stored standard curves, factory-generated
Data output	(dependent on data analysis method)	LCD display Printed alphanumeric hard copy

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT 13 1998

Sheila J. Ramerman
Director, Quality Assurance/Regulatory Affairs
Biocircuits Corporation
1324 Chesapeake Terrace
Sunnyvale, California 94089

Re: K981634
Biocircuits IOS® PSA Test Cartridges and IOS Controls
Regulatory Class: II
Product Code: LTJ
Dated: August 10, 1998
Received: August 11, 1998

Dear Ms. Ramerman:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number: K981634

Device Name: Biocircuits IOS® Prostate Specific Antigen Test Cartridges and IOS PSA Controls

Indications for Use:

The IOS Prostate Specific Antigen Test Cartridges are intended to be used for the quantitative determination of prostate specific antigen in human serum as an aid in the management of patients diagnosed with prostate cancer. They are intended to be used with the Biocircuits IOS® instrument in clinical laboratories, physician office laboratories, and other alternate sites of use close to the point of patient care.

The IOS PSA Controls are to be used to assist in monitoring accuracy and precision in the IOS PSA Test Cartridges.

PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K981634

Prescription Use ✓ OR Over-The-Counter Use ____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)