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

A. 510(k) Number:

k052818

B. Purpose for Submission:

Premarket Notification 510(k) of intention to manufacture and market the Tyson Bioresearch, Inc. EZ SMART-168 Blood Glucose Monitoring System.

C. Measurand:

Whole Blood Glucose

D. Type of Test:

Quantitative, utilizing Glucose Oxidase technology

E. Applicant:

Tyson Bioresearch, Inc.

F. Proprietary and Established Names:

EZ SMART-168 Blood Glucose Monitoring System

EZ SMART-168 Blood Glucose Test Strips

EZ SMART-168 Control Solutions

G. Regulatory Information:

1. Regulation section:

    21 CFR §862.1345, Glucose test system

    21 CFR §862.1660, Single (Specified) Analyte Controls (Assayed and Unassayed)

2. Classification:

    Class II (analyte)

Class I, reserved (controls)

3. Product code:

   NBW (over-the-counter, blood glucose)

   CGA (glucose oxidase, glucose)

   JJX (control material)

4. Panel:

   75 (Chemistry)

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   The EZ SMART-168 Blood Glucose Test Strips are used with the EZ SMART-168 Meter for quantitatively measuring glucose (sugar) in fresh capillary whole blood obtained from the fingertip. The EZ SMART-168 Test Strips are for testing outside the body (in vitro diagnostic use). The EZ SMART-168 Blood Glucose Monitoring System is intended for use in the home and in the professional setting to monitor blood glucose levels for better glucose control among diabetics.

3. Special conditions for use statement(s):

   For over-the-counter use

   This blood glucose monitoring system is not for use for testing blood samples from alternate sites.

   This blood glucose monitoring system is not to be used for Neonatal Testing and is not to be used with critical ill patients.

4. Special instrument requirements:

   EZ SMART-168 Blood Glucose Meter

I. Device Description:

The EZ SMART-168 Blood Glucose Monitoring System contains the following:

1. EZ SMART-168 Blood Glucose Meter
2. EZ SMART-168 Test Strip containing glucose oxidase and potassium ferricyanide
3. Lancets and Lancing device
4. Glucode Chip
5. EZ SMART-168 Glucose Control Solutions are not included with the meter; however 3 levels of control solution are available. The sponsor recommends using a normal and high level control of the user's choice.
6. Carrying Case
7. User's Manual will be included with the meter.
8. Quick Reference Guide
9. Log Book

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VIP International EZ Smart Blood Glucose Monitoring System

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

   k040848

3. Comparison with predicate:

Similarities and Differences		
Item	New Device EZ SMART-168 Blood Glucose Monitoring System k052818	Predicate VIP International EZ Smart Blood Glucose Monitoring System k040848
Measuring Range	20 – 600 mg/dL	20 - 600 mg/dL
Operating Principle	Electrochemical biosensor	Electrochemical biosensor
Intended Use	The EZ SMART-168 Meter is used for in vitro diagnostic use for the quantitative measurement of glucose in fresh capillary whole blood obtained from the fingertip. The EZ SMART-168 Blood Glucose Monitoring System is intended for use in the home and in the professional setting to monitor blood glucose	The EZ Smart Blood Glucose Test Strips are used with the EZ Smart Blood Glucose Meter to measure glucose (sugar) in whole blood. The EZ Smart Test Strips are for testing outside the body (in vitro diagnostic use). The EZ Smart Blood Glucose Monitoring System is intended for use in the home and in

Similarities and Differences		
Item	New Device EZ SMART-168 Blood Glucose Monitoring System k052818	Predicate VIP International EZ Smart Blood Glucose Monitoring System k040848
	levels for better glucose level control among diabetics.	professional settings to monitor blood glucose levels for better glucose level control among diabetics.
Test Principle	Electrochemical Biosensor with Glucose Oxidase	Electrochemical Biosensor with Glucose Oxidase
Operating Temperature	10-40 °C (50-104 °F)	10-40 °C (50-104 °F)
Test Strips	EZ SMART-168 Glucose Test Strip	EZ SMART Glucose Test Strip
Specimen type	Capillary whole blood	Capillary whole blood
Sample volume	≥ 1.5 µL	≥ 1.5 µL
Measuring time	10 seconds	10 seconds
Measuring range	20-600 (mg/dL)	20-600 (mg/dL)
Hematocrit range	35-55%	35-55%
Power source	One 3 V Lithium CR 20322	One 3 V Lithium CR 20322
Strip storage temp	4 to 30 °C (40-86 °F)	4 to 30 °C (40-86 °F)
EMC test standard	EN60601-1-2	EN60601-1-2
Memory storage	Only 28 test results	300 results with date, time, and year stamp
14-Day Average	None, only 28 test average	Calculate 14-day test average
Meter Coding	Check Glucode Chip	Check Strip
Button Design	One Button	Two Button
Meter Dimensions	76 x 47 x 16 (mm)	94 x 49 x 17 (mm)
Weight	44 grams	50 grams
LCD Display	40 x 21.5 (mm)	42 x 41 (mm)

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

EP5-A2 CLSI: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition 2004

EP6-A CLSI: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline Evaluation of Matrix Effects; Approved Guideline, Second Edition 2003

EP7-A CLSI: Interference Testing in Clinical Chemistry; Approved Guideline.

EP9-A CLSI: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline. Vol. 15, No. 17, 1995

FDA Guidance Document Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, May 11, 2005

EN60601-1-2 Electromagnetic Compatibility – Medical electrical equipment

EN61000-4-2 Electromagnetic Discharge

EN61000-4-3 Radiated Electromagnetic Fields

EN61000-4-8 Power frequency Magnetic Immunity Test

IEC 61000-4-3 Electromagnetic compatibility (EMC)

L. Test Principle:

The Test Principle used by this device is electrochemical biosensor technology using Glucose Oxidase. Glucose is oxidized to gluconic acid and electrons are produced from the reaction. The electrons are then trapped by a chemical mediator, potassium ferricyanide. Once the enzymatic reaction is complete, a potential is provided by the meter for a further electrochemical reaction in order to generate a current from the release of trapped electrons. This current is then measured and correlated to the glucose concentration in the whole-blood sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      According to the sponsor precision studies were based on CLSI Document EP5-A2, The following precision results were obtained from spiked venous blood specimens assayed at Tyson Bioresearch, Inc. This study included a measurement of strip-to-strip (within-run) reproducibility by calculating the mean, standard deviation, and % CV for tests conducted on strips from different lots (between-run).

      Whole blood samples from volunteers were collected with heparinized tubes and were spiked with β-D-Glucose to the desired glucose concentration of 30-50 mg/dL, 51-110 mg/dL, 111-150 mg/dL, 151-250 mg/dL, and 251-400 mg/dL. The YSI 2300 glucose analyzer was used to measure the glucose concentrations in venous samples. All measurements were done in "Normal Mode" and a calibration mode of "5/15" (calibrating every 5 measurements or every 15 minutes)

      Results:
      Within Run and Between Run precision of the EZ SMART-168 Test Strips were measured with venous blood samples in the laboratory. The precision data for fifty test strip lots (n = 50) is shown in the tables below:

		EZ SMART-168		
	YSI (mg/dL)	Mean (mg/dL)	SD (mg/dL)	CV%
	45.9	50.6	2.3	4.5
	79.3	81.1	2.9	3.6
Lot 1	120	113	3.3	2.9
	233	226	5.5	2.4
	376	380	12.1	3.2

		EZ SMART-168		
	YSI (mg/dL)	Mean (mg/dL)	SD (mg/dL)	CV%
	49.9	49.7	2.7	5.5
	86.9	86.5	4.2	4.8
Lot 2	130	128	3.9	3.0
	235	237	6.8	2.9
	385	385	8.7	2.3

		EZ SMART-168		
	YSI (mg/dL)	Mean (mg/dL)	SD (mg/dL)	CV%
	44.5	45.6	2.4	5.3
	79.7	82.1	3.3	4.0
Lot 3	118	109	3.2	2.9
	233	237	6.5	2.7
	386	384	9.0	2.3

Within Run Precision of EZ SMART-168 Blood Glucose Monitoring System

Average Glucose Concentration (mg/dL)	49.9	86.9	130	235	385
SD (mg/dL	2.7	4.2	3.9	6.8	8.7
CV%	5.5	4.8	3	2.9	2.3

Between Run Precision of EZ SMART-168 Blood Glucose Monitoring System

Average Glucose Concentration (mg/dL)	46.8	82	123	234	382
SD (mg/dL	2.5	3.5	3.5	6.3	9.9
CV%	5.1	4.1	2.9	2.7	2.6

Variability in tests from strip to strip was 5.1% or less

b. *Linearity/assay reportable range:*

The sponsor indicated that the linearity studies protocol was developed using CLSI

Document, EP6-A. Venous blood was drawn from healthy volunteers and collected into lithium heparin tubes. The blood was then placed in a room temperature environment overnight, until glycolysis occurred and reduced the glucose concentration to nearly zero. The blood was then pooled and allocated to lithium heparin tubes. A small amount of high concentration glucose (10,000 mg/dL) was added to each tube to obtain the desired blood glucose levels needed to perform the test.

Recovery tests were performed by confirming the blood glucose concentration with the YSI 2300. Blood samples with glucose concentrations ranging from 20 to 600 mg/dL were then tested with the EZ Smart Blood Glucose Monitoring System. Three lots of EZ Smart Test Strips, chosen at random, were used during the test. The test results were evaluated to describe recovery over the entire range of blood glucose values. A linear regression analysis was performed by the method of least squares (Y = 0.98X + 3.1, r^2 = 0.9986).

The sponsor's acceptance criteria were: All measurements determined by the EZ Smart System are within a 15% bias of the reference (YSI 2300) results (glucose concentration > 100 mg/dL) and a 15 mg/dL bias of the reference (YSI 2300) results (glucose concentration < 100 mg/dL) see table below:

YSI (mg/dL)	20.0	45.2	80.6	130	230	380	600
Test Results (mg/dL)	23	47	73	120	231	383	584
	24	51	82	127	229	389	588
	22	42	80	135	219	392	600
	25	48	75	126	234	382	596
	20	44	76	128	237	374	575
	23	49	85	124	231	388	600
	20	45	83	137	239	384	570
	26	52	76	129	239	376	581
MEAN	22.88	47.25	78.75	128.25	232.38	383.50	586.75
SD	2.17	3.45	4.33	5.55	6.61	6.23	11.32
CV%	9.47%	7.31%	5.50%	4.33%	2.84%	1.63%	1.93%
Bias%	14.38%	4.54%	2.30%	-1.35%	1.03%	0.92%	-2.21%

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability has been referenced by the manufacturer to ISO 17511.

The three control solutions consist of buffered aqueous solutions of D (+)-glucose containing stabilizers, preservatives, and other non-reactive ingredients. Lot-specific ranges are printed on the EZ Smart-168 Test Strip bottle label. The control values are assigned by repeat testing. Mean values are obtained and ranges are assigned based upon the mean value ± a pre-determined value for each control concentration.

Closed Vial Stability of Control Solution

Control solution stability studies were assessed by the sponsor using accelerated and real time aging studies. Five EZ Smart-168 meters and the YSI 2300 Stat Plus analyzer were used during the testing procedure. The shelf life of closed vial stability claim is 24 months.

Opened Vial Stability of Control Solution

The sponsor conducted open vial stability studies of control solutions (Level 1, 2, and 3) that were stored at room temperature (15°-28° C). Samples were tested every week for 4 consecutive weeks, then every other week for the second month, and every month for the 3rd to 6th months. Five EZ Smart-168 glucose meters and the YSI 2300 STAT PLUS were used during the testing procedure. The open vial stability claim of the control solutions is 3 months after opening.

Closed Vial Stability of Test Strips
According to the sponsor the EZ Smart-168 Test Strips are identical to the previously cleared EZ Smart Test Strips (k040848) that utilize glucose oxidase technology. The test strip stability was assessed using accelerated and real time aging studies. The closed vial glucose test strip stability claim is 24 months.

Open Vial Stability of Test Strips

The open vial stability of Test Strips stored at room temperature (15°-28° C) were performed every week for 4 consecutive weeks, then every other week for the second month, and every month for the 3rd to 6th months. The open vial stability claim for the EZ Smart Test Strips is 3 months when stored as indicated.

d. *Detection limit:*

The detection range from 20 – 600 mg/dL was demonstrated by measuring recovery at the low and high end of the range. See linearity/assay detection limit above.

e. *Analytical specificity:*

According to the sponsor, data were analyzed for chemical interference according to the guidelines given by CLSI document EP7-P. Several compounds were studied to determine if their presence affected the reporting of glucose results in whole blood. Blood samples drawn from healthy donors were collected in to lithium heparin tubes, pooled and mixed. Drugs were added to whole blood to obtain the desired test concentrations. Control samples were made by substituting an equal amount of saline for the volume of drug added to the whole-blood sample, so that the dilutions of the spiked and control samples were identical. The sponsor's results are shown in the table below.

Interferent	Therapeutic Test Level (mg/dL)	High Test Level (mg/dL)	Interferent Level that does not Interfere (mg/dL)
Acetaminophen	2	4	3
Alcohol	---	3500	3500
Ascorbic acid	2	15	7.5
Bilirubin	1.2	20	20
Caffeine	---	100	100
Cholesterol	30	500	500
Creatinine	1.5	30	30
EDTA	---	4	4
Ibuprofen	4.2	40	40
L-Dopa	0.3	2	1
Salicylate	30	125	125
Sodium Fluoride	---	500	500
Tetracycline	0.4	4	4
Tolazamide	2.5	5	3.75
Tolbutamide	10	100	100
Triglyceride	190	2000	2000
Urea	---	5000	5000
Uric acid	7.7	20	20

Acetaminophen, Uric Acid, Ascorbic Acid (vitamin C), and other reducing substances when occurring in normal blood or normal therapeutic concentrations do not significantly affect results. However, abnormally high concentrations in blood may cause inaccurately high results.

Lipemic samples: Cholesterol up to 500 mg/dL or Triglycerides up to 2000 mg/dL do not significantly affect test results. However, glucose values in specimens beyond these levels should be interpreted with caution.

Temperature and humidity studies were conducted by the sponsor to evaluate the EZ SMART-168 meter for acceptable performance after exposure to environmental conditions of 44 °F (7 °C) or 109 °F (43 °C) and 90% relative humidity for 0-12 hours. The sponsors environmental studies were conduced over a temperature range from (10-40 °C) to (50-104 °F) with increasing and decreasing intervals of 5 °C. Samples containing four levels of glucose concentrations (68 mg/dL), (156 mg/dL), (329 mg/dL), and (446 mg/dL) were used. Values obtained were averaged and standard deviations were calculated and the results were compared with those from the YSI 2300 glucose analyzer performed at room temperature (23 °C). The sponsor defined a significant deviation from the reference result as a result larger than 10% bias from the YSI result. The claimed operating range is 10 – 40 ˚C and 10 – 90% relative humidity.

Altitude studies were conducted by the sponsor at 164 feet, 7545 feet and 9875 feet above sea level. Venous samples from healthy volunteers were collected into EDTA tubes and allocated into 2 ml vials. A small amount of glucose high concentration (10,000 mg/dL) was added to each vial to obtain the desired glucose levels of 70 mg/dL, 150 mg/dL, 330 mg/dL, and 400 mg/dL. The samples were then tested using the EZ SmART-168 Blood Glucose Monitoring System and YSI 2300 analyzer. A linear regression analysis was performed by the method of least squares. The Bias % results of the EZ SMART-168 Test Strip by venous blood at different altitudes are shown in the table below.

Altitude (feet)	70 mg/dL	150 mg/dL	250 mg/dL	330 mg/dL	400 mg/dL
164	10.5%	-2.2%	-3.4%	-1.2%	1.9%
7545	3.2%	-4.2%	-11.9%	-6.0%	-4.7%
9875	16.3%	6.8%	14.0%	16.3%	22.1%

The sponsor determined from the above results that the Bias % is below ± 15% when the altitude is below 7545 feet. Based on the sponsor's criteria the EZ SMART-168 Blood Glucose Monitoring System should not be used at altitudes above 7545 feet.

f. *Assay cut-off:*

Not Applicable for this type of device.

2. Comparison studies:

a. *Method comparison with predicate device:*

The sponsor compared the clinical accuracy of the EZ Smart-168 Blood Glucose Monitoring System to the predicate EZ Smart Blood Glucose Monitoring System (k040848) and the YSI 2300 Stat Plus Glucose Analyzer. A 100 patient in house consumer study was performed at QC laboratory in Tyson Bioresearch Inc. to assess the readability of the user's manual, testing accuracy, and user's satisfaction of the EZ Smart-168 Blood Glucose Monitoring System.

The patient profiles were recorded by the technician consisting of sex, age and education. The technician provided the subject with the EZ Sart-168 User's Manual and quick reference guide and asked the subject to perform a glucose test based on the instructions provided. The subject then performed their own finger stick and ran the test with the EZ Smart-168 glucose meter and the predicate EZ Smart meter from the original finger stick and record their results on the questionnaire provided.

The technician then performed the test with the EZ Smart-168 and predicate EZ Smart meter using blood from the original fingerstick and recorded the results. The technician then collected a venous blood sample from the subject for analysis on the YSI 2300 Stat Plus analyzer. The subject was then required to complete the

questionnaire. A linear regression analysis against the YSI 2300 Stat Plus was performed by the method of least squares.

EZ Smart-168 Blood Glucose Monitoring System

N = 100	Lay User	Technician	Lay User/ and Technician
Slope	0.98	0.99	1.00
Intercept	2.6	3.5	2.6
r^2	0.9380	0.9702	0.9833

Clarke's Error-Grid Analysis

The sponsor determined the clinical accuracy of the estimation of glucose concentrations measured by the blood glucose monitors using the error-grid analysis proposed by Clarke et al. The table below outlines the percentage of samples that fell within each portion of the grid:

	Total Points	A	B	C	D	E
Lay User	100	99.0%	1.0%	0.0%	0.0%	0.0%
Technician	100	100%	0.0%	0.0%	0.0%	0.0%

b. *Matrix comparison:*

Not Applicable - finger stick capillary whole blood only.

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):*

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The sponsor's Expected values/Reference ranges were derived from published literature.

The Normal fasting blood glucose range for a non-diabetic adult is 70-110 mg/dL (3.9 to 6.1 mmol/L). One to two hours after meals, normal glucose values should be less than 120 mg/dL (6.7 mmol/L). Consult your physician or healthcare professional for the target glucose values that are right for you.

Expected blood glucose levels for people without diabetes:

Time	Range mg/dL	Range mmol/L
Before breakfast	70-105	3.9-5.8
Before lunch or dinner	70-110	3.9-6.1
1 hour after meals	Less than 160	Less than 8.9
2 hours after meals	Less than 120	Less than 6.7
Between 2 and 4 AM	Greater than 70	Greater than 3.9

N. Instrument Name:

Tyson Bioresearch, Inc. EZ Smart-168 Blood Glucose Monitoring System

O. System Descriptions:

1. Modes of Operation:

   Manual operation

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ____X____ or No _____

3. Specimen Identification:

   Manual identification is used. The memory will store 28 Patient Tests, 28 days Test Average

4. Specimen Sampling and Handling:

   A fresh capillary sample is taken from the fingertip and used immediately. Refer to the Tyson Bioresearch, Inc. EZ Smart-168 Blood Glucose Monitoring System User's Manual for the test procedure.

5. Calibration:

   Lot Specific adjusted calibration with the Check Glucode Chip.

6. Quality Control:

The EZ Smart-168 control solutions are used to check the performance of the EZ Smart-168 meter, Test Strips, and testing technique. The EZ Smart-168 Blood Glucose Monitoring System is performing correctly if the control solution test results fall within the specific control solution range listed on the EZ Smart-168 Test Strip Vial.

Note: EZ Smart-168 Control Solutions are required but not supplied with Test Strips for checking the system. There are three aqueous EZ Smart-168 Control Solutions (Low, Normal, and High) that are available for the user to choose from. The sponsor recommends the use of at least a normal and high control solution to check the accuracy of the system. For more information about the EZ Smart-168 Control Solution, see the EZ Smart-168 Control Solution package insert.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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