

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

A. 510(k) Number:

k062347

B. Purpose for Submission:

Modifications to the predicate meter and test strips

C. Measurand:

Whole Blood Glucose

D. Type of Test:

Quantitative

E. Applicant:

Bayer HealthCare, Diabetes Care

F. Proprietary and Established Names:

Ascensia BREEZE®2 Blood Glucose Monitoring System

G. Regulatory Information:

1. Regulation section:
21 CFR §862.1345, Blood Glucose Test System, Over-the-Counter
21 CFR §862.1660, Quality Control Material (assayed and unassayed)
2. Classification:
Class II
Class I, reserved
3. Product code:
NBW, system, test, blood glucose, over the counter
CGA, glucose oxidase, glucose
JJX, single (specified) analyte controls (assayed and unassayed)
4. Panel:
Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):
See Indications for use below.
2. Indication(s) for use:
The Ascensia® BREEZE® 2 Blood Glucose Monitoring System Consisting of the Ascensia® BREEZE® 2 Blood Glucose Meter, Ascensia® BREEZE® 2 Reagent Strips and Ascensia® BREEZE® 2 Control Solution, is for the measurement of glucose in whole blood. The Ascensia® BREEZE® 2 Blood Glucose Monitoring System allows the user an option to use the palm and forearm in addition to the fingertip (testing) to collect

capillary blood for self monitoring of blood glucose within certain conditions as explained in product labeling. The Ascensia® BREEZE® 2 is an Over-The-Counter (OTC) device used by persons with diabetes. Ascensia® BREEZE® 2 is not for use with neonatal blood specimens. The frequent monitoring of blood glucose is an adjunct to the care of persons with diabetes.

3. Special conditions for use statement(s):

Provides plasma equivalent results.

This product is intended for over-the-counter and point-of-care use.

Not for neonatal use.

4. Special instrument requirements:

Bayer Ascensia BREEZE®2 Blood Glucose Monitoring System

I. Device Description:

The Bayer Ascensia BREEZE®2 Blood Glucose Monitoring System consists of: the Ascensia BREEZE 2 Blood Glucose Monitor, Ascensia BREEZE 2 Control Solutions (Low, Normal, and High), and Ascensia BREEZE 2 Blood Glucose Test Strips. The BREEZE 2 meter accepts both the previously cleared Ascensia AUTODISC test strips and the proposed BREEZE 2 test strips.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Ascensia BREEZE Blood Glucose Meter

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

k024062

3. Comparison with predicate:

Changes to the test system include:

Meter: appearance, battery type, increased memory, decreased sample read time (30 seconds to 7 seconds)

Test Strips: decreased sample volume (2.5 uL to 1 uL), changes in the chemical composition (more enzyme and substrate) polymer support matrix, and modification to the autocalibration feature

Controls: slightly different glucose concentrations and different pH

Range: claimed range is 20 – 600 mg/dL

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

The manufacturer of the Bayer Ascensia BREEZE 2 System utilized ISO 15197-2003 “In vitro diagnostic test systems – requirements for blood glucose systems”, and CLSI EP-7A (Interference).

L. Test Principle:

The BREEZE 2 blood glucose test is based on measurement of electrical current caused by the reaction of glucose with the reagents on the electrode of the test strip. The blood sample is drawn into the end of the test strip through capillary action. Glucose in the sample reacts with glucose oxidase and potassium ferricyanide, generating a current that is proportional to the glucose concentration in the sample. The result is shown on the meter display.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Initially, the sponsor established the equivalence of BREEZE and BREEZE 2 meters by comparing performance characteristics of the original BREEZE meter (k024062) and the proposed BREEZE2 meters (k062347). Previously cleared 30-second AUTODISC test strips were used in these studies. The sponsor then established the performance characteristics of the BREEZE 2 System (the combination of the new meter and the new BREEZE 2 test strips). Results of these two sets of studies are shown below:

a. *Precision/Reproducibility:*

Within day precision of the BREEZE 2 meter was established by testing spiked or glycolized venous blood samples with AUTODISC test strips across the claimed system test range, 20 – 600 mg/dL. Each sample was tested three times on eight separate meters (n = 24). The same samples were run concurrently on YSI and the predicate BREEZE meter. Results of the BREEZE 2/AUTODISC testing are shown in the table below:

BREEZE 2/AUTODISC Within-day Precision

YSI (mg/dL)	Mean BREEZE 2 Value (mg/dL)	Std Dev	CV	Meter to meter bias
20	24	2.6	10.8 %	-4.0 %
66	69	3.9	5.7%	-1.4 %
136	139	5.0	3.6%	-1.9 %
265	269	7.6	2.8 %	-1.7 %
536	551	12.4	2.3 %	-0.8 %
662	692	21.4	3.1 %	0.8 %

Between day precision was assessed by testing 16 BREEZE 2 meters over 10 days; each day low, normal and high BREEZE 2 control solutions were tested once on each meter (n = 160 per level). Results are shown in the table below:

BREEZE 2/AUTODISC Between-day precision

Level	Grand Mean	Pooled StdDev	Pooled CV
Low	67	3.0	4.5 %
Normal	137	3.9	2.8 %
High	315	7.0	2.2 %

The within-day precision of the BREEZE 2 meter system (BREEZE 2 meter and BREEZE 2 strips) was assessed in a laboratory study that used pooled venous blood samples spiked at five different glucose concentrations. For each blood sample, 100 glucose readings were taken (10 readings each on 10 meters). The following table summarizes the average and pooled within-meter percent coefficient of variation (%CV) at each level:

BREEZE 2 System Within Run Precision

Mean	59 mg/dL	118 mg/dL	162 mg/dL	282 mg/dL	457 mg/dL
% CV	4.1 %	2.3 %	2.1 %	1.9 %	2.3 %

Between day precision of the BREEZE 2 meter system was assessed by testing three strip lots on 16 BREEZE 2 meters over 10 days; each day each lot of strips was tested once per meter with low, normal and high BREEZE 2 control solutions (n = 160 per level per lot). Results are shown in the table below:

BREEZE 2 System Between-day precision

Level	Lot	Grand Mean	Pooled Std Dev	Pooled CV
Low	1	52	1.8	3.5 %
	2	52	2.0	3.9 %
	3	53	1.9	3.6 %
Normal	1	108	2.7	2.5 %
	2	107	2.8	2.6 %
	3	107	2.7	2.6 %
High	1	268	6.0	2.2 %
	2	266	6.7	2.5 %
	3	261	5.8	2.2 %

b. Linearity/assay reportable range:

A laboratory study tested the linearity of the BREEZE 2 meter using the AUTODISC: see the precision section above for sample and testing description. Regression analysis showed a linear relationship between BREEZE 2/AUTODISC and the YSI method ($y = 1.024x + 1.25$, $R^2 = 0.999$) and between the BREEZE 2/AUTODISC and the predicate BREEZE meter/AUTODISC ($y = 0.997x - 2.684$, $R^2 = 0.999$).

Linearity of the BREEZE 2 system was established by testing three lots of BREEZE 2 test strips with spiked or glycolized venous blood samples across the claimed system test range, 20 – 600 mg/dL. Each sample was tested ten times on five separate meters (n = 50, 250 total samples). The same samples were tested in duplicate with YSI; the average was considered the YSI value. Regression analysis showed a linear relationship between BREEZE 2 system and the YSI method for each lot:

Test Strip Lot #	Slope	R ²
A	$y = 1.013x - 0.859$	0.999
C	$y = 1.009x - 1.016$	0.999
E	$y = 0.986x + 2.915$	0.999

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

Stability: Accelerated stability data testing suggests that the BREEZE 2 test strip and control solutions have an 18 month shelf life. Real-time stability studies are ongoing.

Each level of Ascensia BREEZE 2 control is prepared gravimetrically and compared

to a commercially available hexokinase glucose reagent kit traceable to a NIST method.

d. Detection limit:

The performance of the test system at the low end of the measuring rang (20 mg/dL) was demonstrated as part of the linearity study. The operating range of the meter is 20 – 600 mg/dL.

e. Analytical specificity:

Potential endogenous and exogenous interferents of the Ascencia BREEZE 2 system were tested in a dose-response manner following CLSI EP7-A guidelines. Aliquots of the blood were supplemented with glucose to a final concentration of 100 mg/dL and measured on a YSI analyzer. Interferents were prepared with an appropriate solvent, and spiked into the 100 mg/dL blood. A control pool was prepared by supplementing the blood with solvent minus the interferent. A series of four to five levels that included the maximum concentration of the substance that would be expected to be encountered in clinical practice were used for each substance. The interferent effect was calculated from the linear relationship between the tested concentrations of each substance.

Albumin, cholesterol, galactose, glipizide, glucosamine, maltose, maltotriose, maltotetraose, metformin, salicylate, triglycerides, and xylose showed no significant bias ($< \pm 10\%$) at any concentration tested. The table below shows the effect of the common interferents that biased the results of the BREEZE 2 system. Shown is the calculated amount of interference at the upper end of normal or therapeutic levels:

BREEZE 2: Calculated Interference at High-Normal or High Therapeutic Levels

Interferent	Upper End Therapeutic or Normal Range (mg/dL)	Calculated percent interference
Acetaminophen	2 mg/dL	4 %
Ascorbic acid	2 mg/dL	1.9 %
Bilirubin	1.2 mg/dL	0.6 %
Dopamine	0.04 mg/dL	0.1%
Gentisate	0.6 mg/dL	1.1 %
Iodoacetate	50 mg/dL	8.2 %
L-dopa	0.3~10 mg/dL	1.2 %
Methyl dopa	0.5 mg/dL	3.2 %
Tolazamide	2.5 mg/dL	6.0%
Uric acid	7.7 mg/dL	4.9 %

Hematocrit

The effect of sample hemoglobin variation on the BREEZE 2 system was tested experimentally by collecting fresh capillary samples from 50 diabetic donors; samples were tested on the BREEZE 2 system and by YSI as the reference method.

Hematocrit was also determined. Glucose levels of the samples ranged from 67 to 635 mg/dL; hematocrit levels ranged from 30 to 55%. Percent assay bias (from YSI) was determined as a function of the hematocrit; the system was determined to have an average 0.72% change in the reported glucose value for every percent deviation in the sample hematocrit from 40%. For example, samples with a 20% hematocrit are calculated to have a + 13% bias while samples with a 55% hematocrit are calculated to have a – 12% bias.

Temperature

Temperature studies for the Ascencia BREEZE 2 Blood Glucose Monitoring System demonstrate that the instrument performs acceptably over the allowable operating range of the meter (10°C to 45°C or 50°F to 113°F).

High-Altitude

A simulated high-altitude study was conducted in a hypoxic chamber to simulate high altitude effects on the Ascencia BREEZE 2 system. Two lots of Ascencia BREEZE 2 reagents were used for the simulated altitude study. The altitude study results indicate the Ascencia BREEZE 2 system showed no evidence to suggest a systematic effect due to lack of atmospheric oxygen at 13,500 feet.

f. *Assay cut-off:*
Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

The performance of BREEZE and BREEZE 2 meters were compared by testing clinical samples on the original BREEZE meter and the proposed BREEZE2 meters; previously cleared 30-second AUTODISC test strips were used in these studies.

BREEZE 2 with AUTODISC test strips (30 second read):

An accuracy study compared the BREEZE 2 system to the YSI method using fresh fingerstick blood samples from people with diabetes. Two separate lots of test strips with different program numbers were utilized in the investigation. 109 people and 11 contrived samples were tested in duplicate (n = 240) on the BREEZE 2, BREEZE, and YSI. Glucose levels ranged from 15 - 533 mg/dL and hematocrits ranged from 28-51%. Linear regression analysis of the data yielded the results below:

Lot 1 vs. YSI	$y = 1.00x + 3.7$	$R^2 = 0.983$
Lot 2 vs. YSI	$y = 1.01x + 3.2$	$R^2 = 0.989$
BREEZE vs. BREEZE 2	$y = 0.97x - 2.1$	$R^2 = 0.976$

BREEZE 2 with BREEZE 2 strips (7 second read):

The BREEZE 2 system was evaluated at two clinical sites; a total of 201 subjects with diabetes and 8 healthcare providers (HCP) completed the study. Subjects performed two fingersticks and tests; HCPs performed two tests on the subject in parallel. Capillary blood was also collected for evaluation by YSI and for hematocrit. Subjects ranged in age, education, and were about equally divided between males and females; the majority of the participants had Type II diabetes. Three lots of strips were tested at each site. At Site 1 105 participants participated in and completed the study (n = 210 readings). Glucose concentrations ranged from 55.9 to 342.0 mg/dL and hematocrit ranged from 22.5 to 54.5%. At Site 2, 96 participants completed the study but four subjects were deleted from the analysis because of protocol deviations; therefore 92 participants yielded a total of 184 readings. Glucose concentrations ranged from 61.3 to 303.5 mg/dL and hematocrit ranged from 33.5 to 52.8%.

Regression Analysis of Ascensia BREEZE 2 Clinical Studies

Clinical Site	Strip Lot	n	Lay-Users vs. YSI			HCP vs. YSI		
			Equation	r	% w/in 15 mg/20% YSI	Equation	r	% w/in 15 mg/20% YSI
1 (n=105)	A	70	$y = 0.99x + 0.99$	0.97	100 %	$y = 0.96x + 1.23$	0.98	98.6 %
	B	70	$y = 0.93x + 3.97$	0.99	98.6 %	$y = 0.91x + 3.70$	0.99	100 %
	C	70	$y = 0.96x + 2.37$	0.98	98.6 %	$y = 0.95x + 3.42$	0.98	98.6 %
2 (n=92)	A	56	$y = 1.00x - 0.08$	0.98	94.6 %	$y = 0.99x - 0.90$	0.97	100 %
	B	64	$y = 1.01x - 0.58$	0.96	96.9 %	$y = 0.97x + 1.93$	0.98	100 %
	C	64	$y = 0.99x - 0.67$	0.95	95.3 %	$y = 0.99x - 1.03$	0.96	96.9 %

In an in-house clinical study, 100 fingerstick samples from people with diabetes were read in duplicate over two weeks. Duplicate YSI values were obtained from each participant; the average was taken as the YSI value. Samples ranged from 52 – 466 mg/dL; contrived samples were used to extend the tested sample range to 18 – 554 mg/dL. Hematocrits ranged from 28-51%. One strip lot was used. Linear regression analysis of the data yielded the following relationship: $y = 1.001x - 0.99$, $R^2 = 0.987$

Alternate Site Testing with the BREEZE 2 System:

The performance of the BREEZE 2 system for testing glucose values from alternate sites was assessed in an in-house study of 60 subjects (57 diabetics, 3 non-diabetics). Participants were predominately female, Caucasian, and Type 2 diabetics; age varied. Subjects claimed to be in a glucose steady state having not eaten, taken diabetes medication, or exercised vigorously for two hours prior to the study; steady state was not confirmed independently. The median fingertip BREEZE 2 blood glucose result for the 60 study subjects was 120 mg/dL, with results ranging from 65.5 to 323.5

mg/dL. The median hematocrit of the subject blood samples was 40% with results ranging from 33.5 to 49.5%.

The BREEZE 2 alternate site claim is limited to the palm and forearm. Therefore study participants performed tests in duplicate on these sites and on the fingertip (n = 6 per subject). A phlebotomist performed separate punctures for the fingerstick, forearm, and two sites on the palm (n = 8 per subject) and collected capillary blood to determine hematocrit. Not all sampling attempts were successful so the total number of samples available for analysis is 222 samples from the palm and 213 from the forearm. Values obtained from the alternate site testing were compared to fingerstick results; linear regression analysis yielded the following results:

Regression Analysis of BREEZE 2 AST Sites Compared to Fingerstick

AST Site	Slope	r	W/in 15mg/ 20%
Palm (n = 222)	$y = 1.01x + 2.25$	0.99	99.1 %
Forearm (n = 213)	$y = 1.00x + 4.00$	0.97	96.2 %

b. *Matrix comparison:*
Not applicable.

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 Ascensia® BREEZE® 2 Blood Glucose Monitoring System labeling states that the standard medical practice goals for a typical non-pregnant individual with diabetes are:

- Before a meal: 90 to 130 mg/dL
- 2 hours after a meal: less than 180 mg/dL

These expected values are referenced from an American Diabetes Association document entitled, “Standards of Medical Care for Patients with Diabetes Mellitus (Position Statement).

N. Instrument Name:

Ascensia® BREEZE® 2 Blood Glucose Monitoring System

O. System Descriptions:

1. Modes of Operation:

The Ascencia® BREEZE® 2 Blood Glucose Monitoring System used with the Ascencia® BREEZE® 2 Reagent Strips and Ascencia® BREEZE® 2 Control Solution is a single use test system used to quantitatively measure blood glucose levels, also known as blood sugar, from fresh capillary whole blood samples taken from the fingertips, palm, or forearm. The Ascencia® BREEZE® 2 Blood Glucose Monitoring System is for in vitro diagnostic use only. The Ascencia® BREEZE® 2 Blood Glucose Monitoring System is not intended for use with neonates.

2. Software:

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

Yes or No

3. Specimen Identification:

The Ascencia® BREEZE® 2 Blood Glucose Monitoring System memory will store 420 results.

4. Specimen Sampling and Handling:

Refer to the Ascencia® BREEZE® 2 Blood Glucose Monitoring System User's Manual.

5. Calibration:

The Ascencia® BREEZE® 2 Blood Glucose Monitoring System, like its predecessors Ascencia® DEX® and Ascencia® BREEZE® meters, uses an automatic calibration system to calibrate the meter for each lot of test strips. The test strips are tested at the manufacturer at the time they are released. Based on performance characteristics for each lot of strips they are assigned a program number from 1 to 73. These program numbers represent the slope and intercept characteristics for each of the lots. The program number is then embedded in a digital label that is applied to the top of each 10-strip reagent disc. When the customer puts the reagent disc into the meter, the meter reads the label and the program number is automatically placed in the meter memory and used for that disc

6. Quality Control:

Three Ascencia BREEZE 2 Controls Solutions are available: low, normal, and high that correspond to whole blood glucose concentrations of approximately 50, 100, and 270 mg/dL respectively. A control test, using an Ascencia® BREEZE® 2 Control, can be used to check the meter and test strips performance. The meter test strips and testing technique are acceptable if the control test result falls within a specific control range. Users are instructed to follow the illustrated directions in the BREEZE® 2 User Guide. Quality control testing should be performed as required by the user's institution's quality control policy or local regulatory requirements.

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.