

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

A. 510(k) Number:

k151611

B. Purpose for Submission:

New device

C. Measurand:

Whole blood glucose

D. Type of Test:

Quantitative, amperometric method, Glucose dehydrogenase (FAD)

E. Applicant:

LifeScan Europe

F. Proprietary and Established Names:

OneTouch Ultra Plus Flex Blood Glucose Monitoring System

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1345, glucose test system

2. Classification:

Class II

3. Product code:

NBW

LFR

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indication(s) for use below.

2. Indication(s) for use:

The OneTouch Ultra Plus Flex Blood Glucose Monitoring System is intended to be used for the quantitative measurement of glucose (sugar) in fresh capillary whole blood samples drawn from the fingertip. The OneTouch Ultra Plus Flex Blood Glucose Monitoring System is intended to be used by a single patient and should not be shared.

OneTouch Ultra Plus Flex Blood Glucose Monitoring System is intended for self-testing outside the body (in vitro diagnostic use) by people with diabetes at home as an aid to monitor the effectiveness of diabetes control. The OneTouch Ultra Plus Flex Blood Glucose Monitoring System is not to be used for the diagnosis of or screening of diabetes, or for neonatal use.

The OneTouch Ultra Plus Test Strips are for use with the OneTouch Ultra Plus Flex Blood Glucose Meter to quantitatively measure glucose drawn from the fingertips.

3. Special conditions for use statement(s):

For over-the-counter use

- The OneTouch Ultra Plus Flex™ Blood Glucose Monitoring System is intended to be used by a single patient and should not be shared.
- The OneTouch Ultra Plus Flex™ System is not to be used for the diagnosis or screening of diabetes or for neonatal use.
- The OneTouch Ultra Plus Flex™ System is not for use on critically ill patients, patients in shock, severely dehydrated patients or hyperosmolar patients (with or without ketosis).
- The OneTouch Ultra Plus Flex™ System is not recommended for alternate site testing (AST).
- The OneTouch Ultra Plus Flex™ Blood Glucose Monitoring System should not be used within 24 hours of receiving a D-xylose absorption test as it may cause inaccurately high results.

- Do Not use the OneTouch Ultra Plus Flex™ Meter when PAM (Pralidoxime) is known or suspected to be in the whole blood sample.

4. Special instrument requirements:

OneTouch Ultra Plus Flex Blood Glucose Meter

I. Device Description:

The OneTouch Ultra Plus Flex Blood Glucose Monitoring System consists of the following components:

- OneTouch Ultra Plus Flex Meter
- OneTouch Ultra Plus Level 3 Control Solution (available separately)
- OneTouch Ultra Plus Level 4 Control Solution (available separately)
- OneTouch Ultra Plus Test Strips (available separately)
- OneTouch Delica Lancing Device (or alternative Lancing Device)
- OneTouch Delica Sterile Lancets (or alternative sterile lancets)
- Carrying Case
- OneTouch Ultra Plus Flex Product Labeling (Owner's Manual and Quick Start Guide)

The OneTouch Ultra Plus Flex Blood Glucose Monitoring System can transmit blood glucose measurement data to a computer or mobile device via a Bluetooth Low Energy transmitter in the meter or via an external USB cable.

Each vial of test strips contains 50 test strips. Each test strip has the following reagent composition: Flavin adenine dinucleotide dependent glucose dehydrogenase (FAD-GDH) from *Aspergillus* sp. – 2 U; potassium ferricyanide 41µg; and other ingredients (buffer, etc.).

The OneTouch Ultra Plus Flex Control Solutions were previously cleared in k131363.

J. Substantial Equivalence Information:

1. Predicate device name(s):

OneTouch Verio Blood Glucose Monitoring System

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

k131363

3. Comparison with predicate:

Item	Candidate Device OneTouch Ultra Plus Flex Blood Glucose Monitoring System	Predicate Device OneTouch Verio Blood Glucose Monitoring System (k131363)
Indications for use	It is intended to be used for the quantitative measurement of glucose in fresh capillary whole blood as an aid to monitor the effectiveness of diabetes control.	Same
Sample type	Whole capillary blood from fingertip	Whole capillary blood from fingertip, forearm, palm
Test strip used	OneTouch Ultra Plus Test Strips	OneTouch Verio Test Strips
Control solutions used	OneTouch Ultra Plus Level 3 and Level 4 Control Solutions	OneTouch Verio Level 3 and Level 4 Control Solutions
Detection method	Amperometric	Same
Enzyme	Flavin adenine dinucleotide dependent glucose dehydrogenase	Same
Sample volume	0.4 µL	Same
Operating conditions	50°F to 104°F (10°C to 40°C) and relative humidity between 10 to 90% R.H.	Same
HCT range	20-60%	Same
Detection range	20-600 mg/dL	Same
Measuring time	5 seconds	Same
Power battery	3V Li battery (CR2032)	Same
Memory storage	500 control and glucose results	Same
Range Indicator	The device includes a monochrome arrow on the LCD display that will point to a pre-printed Red, Green, or Blue range indicator adjacent to the meter lens, corresponding to High, In Range, or Low indication of glucose test values	Not available

	compared to customer-selected target range values.	
Data Download	USB or Bluetooth Low Energy transmitter	USB only
Compatible off-meter software accessories	OneTouch Diabetes Management Software, OneTouch Zoom Pro, OneTouch Reveal	OneTouch Diabetes Management Software
Software	Bias corrected Gemini Blood Glucose algorithm	Gemini Blood Glucose algorithm
	Manual sample tagging of sample type (blood vs. control solution)	Autodetection of sample type (blood vs. control solution)

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

CLSI EP05-A2 “Evaluation of Precision Performance of Quantitative Measurement Methods”

CLSI EP06-A “Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach”

CLSI EP07-A2 “Interference Testing in Clinical Chemistry”

CLSI EP09-A2 “Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline”

L. Test Principle:

The OneTouch Ultra Plus Flex Blood Glucose Monitoring System employs flavin adenine dinucleotide glucose dehydrogenase (FAD-GDH) enzyme chemistry as the standard dry reagent assay for glucose in whole blood. This enzyme assay, with a redox chemical “mediator” reaction, is used to generate an electrical current proportional to the glucose concentration in the blood sample. The system is designed as an amperometric measurement device using current generated from the redox reaction as the measurable response.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The sponsor performed repeatability (within-run) precision studies using venous

whole blood spiked to 7 different glucose concentration levels (15 to 25, 30 to 50, 51 to 110, 111 to 150, 151 to 250, 251 to 400, 570 to 630 mg/dL). Each glucose concentration level was analyzed in replicates of 10, with 3 test strip lots, and 10 meters, for a total of 300 tests per glucose level for each meter. Results are summarized below:

Glucose Level, mg/dL	Strip Lot	n	Average Glucose mg/dL	SD, mg/dL	CV, %
15-25	1	100	19.95	0.55	2.74
	2	100	19.35	0.51	2.63
	3	100	18.88	0.60	3.19
	Combined			0.55	2.86
30-50	1	100	35.07	0.84	2.40
	2	100	34.91	0.92	2.64
	3	100	34.97	0.82	2.34
	Combined			0.86	2.46
51-110	1	100	99.96	1.92	1.92
	2	100	98.76	1.88	1.91
	3	100	97.70	1.86	1.87
	Combined			1.89	1.91
111-150	1	100	135.45	2.53	1.87
	2	100	145.01	3.62	2.50
	3	100	137.33	2.55	1.85
	Combined			2.95	2.11
151-250	1	100	225.92	4.30	1.90
	2	100	219.48	4.30	1.96
	3	100	221.56	4.22	1.91
	Combined			4.28	1.92
251-400	1	100	394.41	8.25	2.09
	2	100	378.96	8.98	2.37
	3	100	373.09	7.07	1.89
	Combined			8.14	2.13
570-630	1	100	665.17	13.49	2.03
	2	100	625.42	12.93	2.07
	3	100	633.23	14.09	2.22
	Combined			13.51	2.11

Intermediate (between run) precision was evaluated using 5 levels of glucose control solutions (0 to 24, 25 to 49, 102 to 138, 298 to 403, 446 to 604 mg/dL) over 10 days with 3 test strip lots. For each level, on each day, 10 meters were used for testing, with 2 replicates collected per meter for a total of 20 replicates per day for each glucose level. Results are summarized below:

Intermediated precision:

Glucose Level, mg/dL	Strip Lot	n	Average Glucose (mg/dL)	SD, mg/dL	CV, %
0-24	1	200	12.57	0.46	3.70
	2	200	12.51	0.46	3.65
	3	200	12.09	0.47	3.92
	Combined			0.47	3.76
25-49	1	200	37.27	1.04	2.78
	2	200	36.55	0.92	2.52
	3	200	36.79	0.94	2.55
	Combined			0.97	2.62
102-138	1	200	119.09	2.30	1.94
	2	200	116.74	1.92	1.64
	3	200	118.11	2.34	1.98
	Combined			2.19	1.86
298-403	1	200	356.52	8.05	2.26
	2	200	347.51	7.78	2.24
	3	200	352.21	7.94	2.25
	Combined			7.92	2.25
446-604	1	200	523.95	14.58	2.78
	2	200	515.06	11.19	2.17
	3	200	522.68	11.78	2.25
	Combined			12.60	2.42

b. Linearity/assay reportable range:

Linearity testing was performed using venous whole blood samples from 9 donors. The evaluation was conducted with 8 meters and 3 test strip lots. Samples with the following glucose concentrations were prepared and confirmed by a laboratory

reference method (YSI): 22.07, 60.94, 101.0, 201.53, 301.71, 401.57, 504.63, 604.74, and 705.94 mg/dL. The study includes a total of 144 testing of samples per glucose concentration per test strip lot using 8 meters, and a total of N=432 measurements per glucose concentration with three test strip lots.

The evaluation yielded the following regression equation based on all samples:

Lot	Slope	y-intercept	R ²
1	1.049	-4.588	0.998
2	1.032	-4.060	0.998
3	1.047	-5.374	0.998

The results of the study support the sponsor's claimed glucose measuring range of 20 – 600 mg/dL.

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

The system is traceable to NIST SRM #917b reference material and calibrated to be plasma-equivalent.

Test strip stability:

Real time stability studies are ongoing to assess the shelf-life and open-vial stability of the OneTouch Ultra Plus Test strips. Real-time stability protocols and acceptance criteria were evaluated and found to be acceptable to support closed-vial stability of 12 months at 41-86°F (65% relative humidity) and open-vial stability of 6 months when test strips are stored at the recommended storage temperature range of 41-86°F and 65% relative humidity.

Control Solution Value Assignment and Stability:

The OneTouch Ultra Plus Control Solutions were previously cleared under k120708. Stability studies support a closed-vial shelf life of 24 months and an open-vial shelf life of 6 months when stored at 41- 86° F.

d. Detection limit:

The reportable range for the OneTouch Ultra Plus Flex Blood Glucose Monitoring System is 20 to 600 mg/dL supported by the linearity assay study above (M.1.b).

e. Analytical specificity:

Interference studies were performed by spiking endogenous and exogenous substances into venous whole blood. Each potential interferent was tested with 3 test strip lots at 2 glucose levels (70 and 300 mg/dL) for a total of 96 samples (12 replicates per lot per

interferent level). Results of test samples measured on the OneTouch Ultra Plus Flex Blood Glucose Meter System were compared to the mean of the control sample measured on the OneTouch Ultra Plus Flex Blood Glucose Meter System and the bias calculated. Significant interference is defined by the sponsor as a bias within $\pm 10\%$ compared to a control sample.

The sponsor claims no significant interference for the substances and concentrations shown in the table below:

Substance	Highest Concentration tested with no observed interference
Acetaminophen	10.89 mg/dL
Ascorbic acid	6.38 mg/dL
Bilirubin	20.53 mg/dL
Cholesterol	794.4 mg/dL
Creatinine	31.83 mg/dL
Dopamine	0.051 mg/dL
EDTA	0.10 mg/dL
Ephedrine	0.21 mg/dL
Galactose	60.39 mg/dL
Gentisic Acid	1.85 mg/dL
Glutathione	92.61 mg/dL
Hemoglobin	237.60 mg/dL
Heparin	2.15 mg/dL
Ibuprofen	50.52 mg/dL
Icodextrin	1241.72 mg/dL
Lactose	4.25 mg/dL
L-Dopa (Levo-Dopa)	1.01 mg/dL
Maltose	363.60 mg/dL
M-Dopa (Methyl-Dopa)	1.50 mg/dL
Salicylic Acid	58.90 mg/dL
Tetracycline	1.52 mg/dL

Tolazamide	15.03 mg/dL
Tolbutamine	65.98 mg/dL
Triglycerides	3431.11 mg/dL
Urea	297.55 mg/dL
Uric Acid	8.10 mg/dL

The sponsor lists the following limitations in the Owner’s Manual and the Test Strip Insert:

- The OneTouch Ultra Plus Flex™ Blood Glucose Monitoring System should not be used within 24 hours of receiving a D-xylose absorption test as it may cause inaccurately high results.
- Do not use the OneTouch Ultra® Plus Flex™ Blood Glucose Meter when PAM (Pralidoxime) is known or suspected to be in the whole blood sample.
- If you have medical conditions that are associated with high uric acid level or hyperuricemia (e.g. gout), then please check with your Doctor before using the One Touch Ultra Plus Flex Blood Glucose Monitoring System. Uric acid at concentrations greater than 8.0 mg/dL can interfere with glucose measurements.
- If you take drugs containing acetaminophen (e.g Tylenol etc.) or Dopamine at doses higher than the recommended high therapeutic level, then you may obtain inaccurate readings from the OneTouch Ultra Plus Flex blood glucose monitoring system. Please check with your Doctor if you are unsure.

f. Assay cut-off:

N/A

2. Comparison studies:

a. Method comparison with predicate device:

To assess system accuracy, results from the OneTouch Ultra Plus Flex Blood Glucose Monitoring System were compared to a reference method (YSI). Capillary fingerstick and venous whole blood samples were obtained by professional users from 113 participants with glucose concentrations ranging from 36.7-507.3 mg/dL. To obtain extreme blood glucose concentrations, 6 samples were altered. Testing was done using 6 meters and 3 test strip lots tested in duplicate. Results of the first test from each participant are shown below:

For glucose concentrations < 75 mg/dL

Within ± 5 mg/dL	Within ± 10 mg/dL	Within ± 15 mg/dL
12/20 (60.0%)	18/20 (90.0%)	20/20 (100%)

For glucose concentrations > 75 mg/dL

Within ± 5 %	Within ± 10 %	Within ± 15 %	Within ± 20 %
58/93 (62.4%)	83/93 (89.2%)	92/93 (98.9%)	93/93 (100%)

Linear regression analysis

Slope	Intercept	R ²	N	Glucose Concentration range (new meter) (mg/dL)
1.02	-2.16	0.99	113	36.7 – 507.3

b. Matrix comparison:

N/A

3. Clinical studies:

a. Clinical Sensitivity:

N/A

b. Clinical specificity:

N/A

c. Other clinical supportive data (when a. and b. are not applicable):

User performance study

To assess the performance of the OneTouch Ultra Plus Flex Blood Glucose Monitoring System in the hands of the intended users, the sponsor performed a study with 169 lay user participants at 4 clinical sites who collected and tested samples from their own fingertip. Results were analyzed by comparing capillary whole blood glucose results obtained by the lay users with the OneTouch Ultra Plus Flex Blood Glucose Monitoring System against results obtained with the same fingerstick blood samples from

the same patients analyzed by a laboratory reference method (YSI). The glucose concentrations in the samples ranged from 49.4 to 571.8 mg/dL as measured by the laboratory reference method. Results are summarized in the tables below:

For glucose concentrations < 75 mg/dL

Within ± 5 mg/dL	Within ± 10 mg/dL	Within ± 15 mg/dL
15/20 (75.0%)	18/20 (90.0%)	19/20 (95.0%)

For glucose concentrations > 75 mg/dL

Within ± 5 %	Within ± 10 %	Within ± 15 %	Within ± 20 %
94/149 (63.1%)	132/149 (88.6%)	143/149 (96.0%)	149/149 (100%)

Linear regression analysis

Slope	Intercept	R ²	N	Glucose Concentration range (new meter) (mg/dL)
1.02	-1.29	0.99	169	49.4 – 571.8

Usability Study:

A usability study was performed to assess the readability of the labeling. 99 lay users were provided the owner’s manual for 4-6 days at home prior to completing a system use evaluation (under study staff observation) followed by a questionnaire designed to evaluate the ease of use of the device and the clarity of the English language labeling. The responses to the Instructions for Use Questionnaire met the acceptance criteria, with lay users demonstrating acceptable levels of comprehension of the user manual and the strip insert. The readability of the labeling using a Flesch-Kincaid analysis was found to be: OneTouch Ultra Plus Flex Owners Booklet (7.7); OneTouch Ultra Plus Test Strip Insert (7.6) and OneTouch Ultra Plus Control Solution Insert (6.9).

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

The sponsor lists the following expected blood glucose levels for non-pregnant people

without diabetes:

Time	Range (mg/dL)
Fasting	Less than 100
2 hours after meals	Less than 140

Source: American Diabetes Association, Standards of Medical Care in Diabetes, Diabetes Care Vol. 38, Supplement 1, S1-S94, January 2015

N. Instrument Name:

OneTouch Ultra Plus Flex Blood Glucose Meter

O. System Descriptions:

1. Modes of Operation:

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes or No

Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

Yes or No

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:

There is no sample identification function with this device. Samples are applied directly to the test strip as they are collected.

4. Specimen Sampling and Handling:

The system is intended to be used with capillary whole blood from fingerstick only. No alternative site testing. The whole blood sample is applied directly to the test strip by capillary action.

5. Calibration:

The OneTouch Ultra Plus Flex Blood Glucose Monitoring System is calibrated such that the result displayed is equivalent to the glucose level in a plasma sample. Calibration is automatic. There is no user input for coding.

6. Quality Control:

Glucose control solutions at two different concentrations can be run with this device. Recommendations on when to test the control materials are provided in the labeling. An acceptable range for each control level is printed on the control solutions vial label. The user is cautioned not to use the meter and to contact customer support if the control result falls outside these ranges.

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

1. Hematocrit Study:

To evaluate the effect of hematocrit on the OneTouch Ultra Plus Flex Blood Glucose Monitoring System, venous blood samples with hematocrit levels of 19%, 30%, 42%, 50%, and 61% were tested at 6 glucose concentrations (40±5, 65±5, 90±5, 120±6, 350±17, and 560±28 mg/dL). The evaluation included 8 meters, each tested with 2 replicates for 3 lots of test strips for a total of 864 measurements per hematocrit level. Results from the meter were compared to results obtained using a laboratory-based reference method (YSI). The evaluation of percent bias relative to YSI demonstrated acceptable performance across the hematocrit range of 20-60%.

2. Altitude study:

To evaluate the effect of altitude on the OneTouch Ultra Plus Flex Blood Glucose Monitoring System, meters were tested at 2 altitudes above sea level (0 ft and 10,000 ft). Venous whole blood samples spiked at 3 glucose levels (70, 240, and 450 mg/dL) were tested at each altitude. The evaluation included 16 meters and 3 test strip lots. Each lot included 2 replicates for a total of 288 measurements per test strip lot. Results were compared to results obtained using a laboratory-based reference method (YSI) and demonstrated that altitudes up to 10,000 feet above sea level have no significant effect on blood glucose measurements from the OneTouch Ultra Plus Flex Blood Glucose Monitoring System.

3. Sample Volume:

To demonstrate the minimum sample volume, 0.2, 0.3, 0.4, and 0.5µL of venous whole blood samples at glucose concentrations of 65 and 450 mg/dL were tested. Testing included 6 replicates from 3 test strip lots for each glucose concentration/sample volume combination for a total of 240 measurements per test strip lot. 1 meter was used during testing. Values obtained were compared to values

obtained using a laboratory-based reference method (YSI). Results support a minimum sample volume of 0.4 µL.

4. Operating Conditions Study:

Temperature and humidity operating conditions were evaluated for temperatures ranging from 41°F to 113°F (5°C to 45°C) and relative humidity between 10 and 90% R.H. using 5 glucose concentration levels of venous whole blood (65, 150, 240, 350, and 450 mg/dL), 6 meters, and 3 lots of test strips over 11 days for a total of 540 measurements per glucose concentration. Individual glucose measurements were compared to the reference method (YSI) and percent bias were calculated. Results demonstrated that glucose measurements on the OneTouch Ultra Plus Flex Blood Glucose Monitoring System were not affected at temperatures ranging from 50°F to 104°F (10°C to 40°C) and relative humidity between 10 to 90% R.H. If the operating temperature is outside of these conditions, the meter displays an error message instead of a blood glucose value.

5. Infection Control and Robustness Studies:

The device is intended for single-patient use only. Disinfection efficacy testing on the surface materials of the meter demonstrated complete inactivation of hepatitis B virus (HBV) with the chosen disinfectant, Clorox Germicidal Wipes, 0.55% sodium hypochlorite (EPA Registration # 67619-12). Robustness studies were also performed by the sponsor demonstrating that there was no change in performance or external materials of the meter after 3316 cleaning and 475 disinfection cycles designed to simulate 4 years of device use with a maximum frequency of cleaning at 1x/day and disinfection at 1x/week. Cleaning and disinfection durability of the OneTouch Delica Lancing Device was previously shown in k131363.

6. EMC testing was certified and a compliance certificate provided.

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.