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

A. 510(k) Number:

k182593

B. Purpose for Submission:

New Device

C. Measurand:

β-Ketone, as beta-hydroxybutyrate, in fingertip capillary whole blood

D. Type of Test:

Quantitative amperometry, βKetone (beta-hydroxybutyrate)

E. Applicant:

Apex Biotechnology Corp.

F. Proprietary and Established Names:

KET-1 Blood Ketone Monitoring System

G. Regulatory Information:

1. Regulation section:

   21 CFR §862.1435, Ketones (nonquantitative) test system

2. Classification:

   Class I, meets the limitation of exemptions 21 CFR §862.9(c)(5)

3. Product code:

   JIN, Nitroprusside, Ketones (urinary, non-quantitative)

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indication(s) for use below.

2. Indication(s) for use:

   The KET-1 Blood Ketone Monitoring system is intended to quantitatively measure β-hydroxybutyrate (β-ketone) in fresh capillary whole blood from fingertips. It should only be used by a single patient and it should not be shared. Testing is done outside the body (In Vitro diagnostic use). It is intended for self-testing by people with diabetes mellitus at home as an aid to monitoring the effectiveness of diabetes control programs. It is not to be used for diagnosis or screening of diabetes, or for neonatal use.

   The KET-1 Blood Ketone Monitoring System is comprised of the KET-1 Blood Ketone Meter and KET-1 Blood Ketone Test Strip.

3. Special conditions for use statement(s):

   - The system should not be used to test neonates
   - Do not test samples other than fresh capillary blood obtained from fingertip.
   - Do not use the system at altitudes above 10,335 feet (3,150meters).
   - Do not use when Hematocrit is outside the acceptable hematocrit range for testing of 20% to 60%.
   - Severe dehydration (excessive water loss) may cause inaccurate results. If you believe you are suffering from severe dehydration, consult your healthcare professional immediately.
   - For in vitro diagnosis use only.
   - Critically ill patients should not be tested with this device.
   - Inaccurate results may occur in severely hypotensive individuals or patients in shock or in a hyperglycemic-hyperosmolar state.
   - Incorrect result may occur in individuals who are dehydrated.
   - The meter and lancing device are for single patient use. Do not share these items with anyone, including other family members! Do not use on multiple patients!
   - Do not reuse; each test strip is for single use only.
   - Do not use when humidity is higher than 90% and lower than 10%, as extremes in humidity may affect results.
   - For single patient use only.
   - For over-the counter use.
   - The system is not intended for use in the diagnosis of or screening for diabetes mellitus.

4. Special instrument requirements:

   KET-1 Blood Ketone Meter

I. Device Description:

The KET-1 Blood Ketone Monitoring System consists of the KET-1 Blood Ketone Meter, KET-1 Blood Ketone Test Strips, and KET-1 Control, solutions (level 1 and Level 2). The system is for self-testing of blood ketone. The KET-1 Blood Ketone Test Strips and KET-1 Ketone Control Solutions are purchased separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Nova Max Plus Blood Glucose and β-Ketone Monitoring System

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

   k091547

3. Comparison with predicate:

Similarities		
Item	Candidate Device KET-1 Blood Ketone Monitoring System k182593	Predicate Device Nova Max Plus Blood Glucose and β-Ketone Monitoring System k091547
Intended use	Quantitatively measure β-hydroxybutyrate (β-Ketone) in fresh capillary whole blood from fingertips as an aid to monitoring the effectiveness of diabetes control programs	Same
Measuring Range	0.1 to 8 mmol/L	Same
Assay method	β -hydroxybutyrate dehydrogenase	Same

Differences		
Item	Candidate Device KET-1 Blood Ketone Monitoring System k182593	Predicate Device Nova Max Plus Blood Glucose and β-Ketone Monitoring System k091547
Hematocrit Range	20%-60%	25%-60%
Analysis Time	8 seconds	10 seconds
Power source	2 X CR2032, 3-volt coin cell battery	1 X CL2450, 3-volt coin cell battery

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

CLSI EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline.
CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.
CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline.

L. Test Principle:

The test principle of KET-1 Blood Ketone Monitoring System is based on the amperometry detection of beta-hydroxybutyrate in whole blood. β-hydroxybutyrate is converted by the enzyme β-hydroxybutyrate dehydrogenase to acetoacetate. The magnitude of electrical current resulting from this enzymatic reaction is proportional to the amount of β-hydroxybutyrate present in the sample. The result is displayed on the meter in mmol/L.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Repeatability

Repeatability was assessed using two ketone concentration ranges (1.2 – 0.6 mmol/L and 1.4 - 2.2 mmol/L) and five lithium heparinized whole blood samples and five lithium heparinized whole blood samples spiked with β-hydroxybutyrate to create concentrations of (0.55, 2.17, 3.76, 6.26, and 7.58 mmol/L) and tested on ten KET-1 meters. Ten replicates were tested per meter per concentration with each of the three lots of the test strips. The results are summarized below:

Concentrations (mmol/L)	N	Men (mmol/L)	SD (mmol/L)	% CV
0.55	300	0.5	0.06	11.8
2.27	300	2.2	0.09	4.2
3.76	300	4.1	0.17	4.2
6.26	300	6.3	0.24	3.7
7.58	300	7.2	0.25	3.4
Level 1 control 0.2-0.6 mmol/L	300	0.5	0.05	11.1
Level 2 control 1.4-2.2 mmol/L	300	1.8	0.06	3.2

Intermediate Precision study:

Intermediate precision was evaluated using three lots of KET-1 blood Ketone Strip

with 10 meters. Two levels of control solutions were used with β-ketone ranges of 0.2-0.6 mmol/L (Level 1) and 1.4-2.2 mmol/L (Level 2). For each control, ten replicates were taken each day for ten days, so that 100 individual measurements were generated per control level. The results from all strip lots are summarized below:

Control Level	N	Mean (mmol/L)	SD (mmol/L)	% CV
1	300	0.5	0.05	11.1
2	300	1.8	0.06	3.2

b. Linearity/assay reportable range:

The Linearity of the KET-1 Blood Ketone Monitoring System was evaluated using Lithium Heparin venous whole blood spiked with β-hydroxybutyrate. Seven whole blood samples were adjusted to the following β-hydroxybutyrate concentrations: 0.04, 0.51, 2.23, 4.12, 6.03, 7.11, and 8.52 mmol/L. The concentrations were assigned using the Beckman Coulter UniCel DxC800 Clinical System with STANBIO β-Hydroxybutyrate LiquiColor Test Kit. The summary of the of the linear regression analysis for each lot was as follow:

Test Strip Lot	Slope	y-intercept	R value
Lot 1	0.9911	0.0158	0.9985
Lot 2	0.9829	0.0338	0.9983
Lot 3	0.9887	0.0265	0.9984

The results of the study support the sponsor's claimed (β-ketone) measuring range of 0.1-0.8 mmol/L.

Validation testing was performed demonstrating that the meter displays 'HI" when the measurement result is greater than 8.0 mmol/L and "LOW" when the measurement result is less than 0.1 mmol/L, as intended.

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

The KET-1 Blood Ketone Monitoring system is traceable to an in-house standard prepared from commercially available control materials.

Test strip stability:
The KET-1 Blood Ketone Test Strip are provided in individual foil packages. The shelf life stability of the foil packaged strips was assessed with real-time testing. The study protocol and acceptance criteria were reviewed and found acceptable to support the sponsor's claimed stability of 18 months when stored under recommended storage conditions of 39°F – 86°F (4-30°C) and relative humidity of 10-85%.

d. Detection limit:

Please refer to Linearity study above, Section M.1.b.

e. Analytical specificity:

To evaluate interference of exogenous and endogenous interfering substances, three lithium heparinized whole blood samples with ketone concentrations of 0.8 mmol/L, 3.3 mmol/L and 5.8 mmol/L were divided into two aliquots: control (with no added interferent) and test (with assessed interferent). Each sample was tested using 10 KET-1 meters and the difference between meter results obtained with the test sample compared to the control samples calculated. The sponsor defined no significant interference as bias within 0.3 mmol/L for β-ketone < 1.5 mmol/L and ≤ 20% for β-ketone ≥1.5 mmol/L. The following table lists the highest tested concentration of each substance at which no significant interference was detected.

Substance	Highest concentration at which no significant interference is observed (mg/dL)
Acetaminophen	20
Acetone	10
Acetoacetate	10
Ascorbic acid	4
Bilirubin	10
Captopril	10
Cholesterol	500
Creatinine	6
Dopamine	2
Glucose	900
Ibuprofen	50
L-DOPA	3
Methyl-Dopa	7.5
N-acetylcysteine	10
Tetracycline	10
Tolazamide	15
Triglyceride	750
Uric acid	20
EDTA	180
Heparin	18IU/mL
Salicylate	60
Tolbutamide	100

f. Assay cut-off:

Not Applicable.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Not applicable. See section M.3.c below for accuracy in the hands of the intended user.

   b. *Matrix comparaison :*

      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):*

      Lay-user accuracy study:

      To assess the performance of the KET-1 Blood meter monitoring system in the hands of the intended users, a lay user study was conducted with 100 lay user participants using one KET-1 Blood meter monitoring system and three lots of. KET-1 test strips. Each lay user participants self-tested their own fingertip capillary blood using the KET-1 Blood meter ketone monitoring system unassisted and were instructed to use instructions provided in the labeling.

      The lay user β-Ketone measurements were compared to those obtained by results obtained trained users with the who used Beckman DxC 800 with the STANBIO β-Hydroxybutyrate LiquiColor Test Kit. The range of β-Ketone concentrations across all subjects was 0.11 to 2.40 mmol/L. Each sample was measured in singlicate. The results are summarized below:

      Results for samples with β-ketone concentration <1.5 mmol/L

Within ± 0.15 mmol/L	Within ± 0.225 mmol/L	Within ± 0.30 mmol/L
92/94 (98%)	94/94 (100%)	94/94 (100%)

      Results for samples with β-ketone concentration ≥1.5 mmol/L

Within ± 10%	Within ± 15%	Within ± 20%
6/6 (100%)	6/6 (100%)	6/6 (100%)

Linear regression analysis of the results:

Sample	Slope	Intercept	R2	N	Ketone Concentration (mmol/L)
Fingertip blood	0.9857	0.0038	0.9837	100	0.11-2.40

Readability Evaluation: The readability of the over-the counter, home use labeling was evaluated using a Flesch-Kincaid analysis and demonstrated that the grade level scores were less than 8th grade.

4. Clinical cut-off**:**

Not Applicable.

5. Expected values/Reference range:

Based on published literature, the sponsor included the following in the labeling:

The normal adult blood β-Ketone range for a person without diabetes is less than 0.6 mmol/L.

A. Rewers, Current Controversies in Treatment and Prevention of Diabetic Ketoacidosis, Advances in Pediatrics 57 (2010) 247–267.

N. Instrument Name:

KET-1 Blood Ketone Monitoring System

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 ___X_____

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

Yes _____ or No ___X_____

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:

   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 KET-1 Blood Ketone Monitoring System is intended to be used with capillary whole blood from the fingertip which is applied directly to the test strip.

5. Calibration:

   There is no calibration required for KET-1 Blood Ketone Monitoring System by the user.

6. Quality Control:

   Two levels of KET-1 Ketone Control Solutions are available and are purchased separately.

P. Other Supportive Instrument Performance Characteristics Data Not Covered in the "Performance Characteristics" Section above:

1. Hematocrit Study:

   The effects of varying hematocrit levels on the measurement of β-ketone concentration was evaluated using venous whole blood samples with hematocrit levels at 20%, 25%, 30%, 40%, 45%, 50% and 60%. Four different with β-ketone concentrations of 0.4-0.6 mmol/L, 1.5-2.5 mmol/L, 3.5-5.4 mmol/L, and 5.0-6.5 mmol/L were prepared at each of the four levels with seven hematocrit levels. The β-ketone concentration was measured using ten KET-1 meters and three test strips. The % bias at each hematocrit level relative to the result obtained STANBIO β-Hydroxybutyrate LiquiColor Test Kit was calculated. The result support the claimed acceptance hematocrit range of 20-60%.

2. Altitude Study:

   An altitude/oxygen dependability study was performed to assess the effect of low oxygen levels when the system is used at elevations above sea level. For testing two levels sea level (0 and 10, 335 feet). Venous whole blood samples at five levels approximately 0.5, 2.0, 4.0, 6.0 and 7.5 mmol/L and two levels of KET-1 control solution were tested at sea level and 10, 335 feet elevation. Twenty ketone readings per ketone level were taken at each of the two elevations. The results demonstrated acceptable bias to support the claim that altitude up to 10, 335 feet have no significance effect on β -Ketone measurement when measured with KET-1 monitoring system.

3. Operating Conditions Study:

The sponsor performed testing in operating condition studies to evaluate the operating temperature and relative humidity (RH) ranges. Venous whole blood samples with β - Ketone concentrations ranges of 0.47 mmol/L, 2.21 mmol/L, 3.76 mmol/L 6.15 mmol/L were tested. Each sample was tested at the combined temperature and humidity conditions shown below using 10 KET-1 meters, and 3 lots of KET-1 test strip. The results obtained on the KET-1 Blood Ketone meter were compared to results obtained using the STANBIO β-Hydroxybutyrate LiquiColor Test Kit.

Temperature	10, 20, 25, 30, 40±2°C at 45-55%RH
Relative Humidity	20%±5% at 10°C and 40^0C
	50%±5% at 25°C
	90%±5% at 10°C and 40°C

The results support the sponsor's claimed operating temperature range of 50-104°F (10°C – 40°C) and 20-90% RH.

4. Sample Volume Study:

A sample volume study was conducted to verify the minimum sample volume required for the KET-1 monitoring system. Venous whole blood samples were tested at 0.6 µL, 0.7 µL, 0.8 µL, 0.9 µL and 10 µL volume. Samples had concentration of (0.50 mmol/L, 3.91 mmol/L, 7.44mmol/L). Testing was performed using 10 test strips for each of three lots of test strips for each test volume and each ketone level. Results from the study support the claimed sample volume of 0.8 µL.

5. Electromagnetic Compatibility:

The sponsor provided documentation certifying that acceptable electromagnetic testing had been performed and the KET-1 Monitoring System was found compliant.

6. Infection Control Studies:

This device system is intended for single-patient use only. Disinfection efficacy studies were previously performed (k131750) on the materials comprising the meter by an outside commercial testing laboratory demonstrating complete inactivation of hepatitis B virus (HBV) with the chosen disinfectant, Clorox Healthcare Bleach Germicidal Wipes (EPA Registration # 67619-12-5813). Robustness testing was conducted by the sponsor demonstrating that there was no change in performance or external materials of the meter after 1825 cleaning and disinfection cycles with Clorox Healthcare Bleach Germicidal Wipes. The robustness studies were designed to simulate 5 years of single-patient use. Labeling was reviewed for adequate instructions for the validated cleaning and disinfection procedures.

Q. Proposed Labeling:

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

R. Conclusion:

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