510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K234063

B Applicant

T2Biosystems, Inc.

C Proprietary and Established Names

T2Candida 1.1 Panel

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PII	Class II	21 CFR 866.3960 - Nucleic Acid-Based Device For The Amplification, Detection, And Identification Of Microbial Pathogens Directly From Whole Blood Specimens	MI - Microbiology
NSU	Class II	21 CFR 862.2570 - Instrumentation for clinical multiplex test systems	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

To amend the T2Candida 1.1 Panel labeling regarding testing with pediatric patients.

B Measurand:

The assay amplifies and detects nucleic acids of the following species:
Candida albicans and/or *Candida tropicalis*
Candida parapsilosis
Candida krusei and/or *Candida glabrata*

C Type of Test:

The T2Candida 1.1 Panel, performed on the T2Dx Instrument, is a molecular diagnostic assay for the detection of the above listed *Candida* species from whole blood specimens obtained from patients with signs and symptoms of invasive *Candida* infection.

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
T2Candida 1.1 Panel and T2Dx Instrument is a qualitative T2 Magnetic Resonance (T2MR) assay for the direct detection of *Candida* species in K_2EDTA human whole blood specimens from patients with symptoms of, or medical conditions predisposing the patient to, invasive fungal infections.

The T2Candida 1.1 Panel identifies five species of *Candida* and categorizes them into the following three species groups:

1. *Candida albicans* and/or *Candida tropicalis*

2. *Candida parapsilosis*

3. *Candida glabrata* and/or *Candida krusei*

The T2Candida 1.1 Panel does not distinguish between *C. albicans* and *C. tropicalis*. The T2Candida 1.1 Panel does not distinguish between *C. glabrata* and *C. krusei*.

The T2Candida 1.1 Panel is indicated for the presumptive diagnosis of candidemia. The T2Candida 1.1 Panel is performed independent of blood culture. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification, and for organisms not detected by the T2Candida 1.1 Panel.

The T2Candida positive and negative External Controls (T2Candida QCheck Positive Kit and the T2Dx QCheck Negative Kit) are intended to be used as quality control samples with the T2Candida 1.1 Panel when run on the T2Dx Instrument. These controls are not intended for use with other assays or systems.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

For In Vitro Diagnostic Use

Device performance was initially established with samples from adult patients. Panel performance with samples from pediatric patients was supported by additional studies with pediatric subjects. Panel performance with samples from neonates has not been established.

D Special Instrument Requirements:

The T2Candida 1.1 Panel is performed on the T2Dx Instrument.

IV Device/System Characteristics:

A Device Description:

The T2Candida 1.1 panel is a qualitative molecular diagnostic assay that detects *Candida* species directly from whole blood. Together with the T2Dx Instrument, the T2Candida 1.1 panel uses whole blood compatible PCR amplification followed by T2 magnetic resonance (T2MR) detection. The T2Dx Instrument was originally evaluated in DEN140019 and is unchanged in this submission.

To initiate testing, at least 3 mL of whole blood specimen is collected into a 4 mL K_2EDTA vacutainer. The sample tube is loaded into the T2Candida Sample Inlet, which is then placed on the T2Candida Base along with the T2Candida Reagent Tray. The Reagent Tray contains the internal control, amplification reagent, enzyme, and the probe-coupled superparamagnetic particles for each *Candida* target. The assembled pack is then inserted in the T2Dx instrument, which executes all steps after specimen loading.

Two milliliters of blood specimen are automatically transferred to the T2Dx Instrument where the red blood cells are lysed, *Candida* cells are concentrated and lysed, and *Candida* DNA is amplified. Amplification products are detected by T2MR detection using species-specific probes which are attached to the superparamagnetic particles. The assay provides an identification of *Candida albicans* and/or *Candida tropicalis*, *Candida parapsilosis*, and *Candida glabrata* and/or *Candida krusei*. The test does not distinguish between *C. albicans* and *C. tropicalis*. The test does not distinguish between *C. glabrata* and *C. krusei*. Results are provided within 5 hours of the initial blood draw.

B Principle of Operation:

The T2Candida Panel and T2Dx Instrument rely on PCR amplification of conserved sequences to detect *Candida* species. The assay includes a single pair of pan-*Candida* primers that hybridize to conserved sequences within the 5.8S and 26S ribosomal RNA operon of *Candida* species and amplify the intervening transcribed spacer 2 sequence (ITS2) from nucleic acid released from the lysed *Candida* cells contained in the specimen. The primers are mixed in a ratio such that an asymmetric product produces a predominantly single stranded nucleic acid after amplification. The primers are designed to also amplify the internal control. Species-specific and internal control-specific probes provide the specificity of the assay.

The instrument detects the amplified PCR product directly in the whole blood matrix by amplicon-induced agglomeration of superparamagnetic particles attached to the species-specific and internal control-specific probes. The detection method measures the spin-spin relaxation signals of water molecules. For these measurements, the T2Dx Instrument utilizes a small permanent magnet and a specialized radio frequency coil to measure the T2MR signal from the water molecules. T2MR measures the disorder of the nuclear spins of the water molecules

contained in the sample and this disorder is directly proportional to the superparamagnetic particle clustering state. The T2Dx Instrument reports a positive or negative result for each detection channel: *C. albicans/C. tropicalis* (A/T), *C. parapsilosis* (P), *C. krusei/ C. glabrata* (K/G) and internal control (IC).

V Substantial Equivalence Information:

A Predicate Device Name(s):
T2Candida 1.1 Panel

B Predicate 510(k) Number(s):
K173536

C Comparison with Predicate(s):

Device & Predicate Device(s):	**Device: T2Candida 1.1 Panel** K234063	**Predicate: T2Candida 1.1 Panel** K173536
Device Trade Name	T2Candida 1.1 Panel	T2Candida 1.1 Panel
General Device Characteristic Similarities		
	Device: K234063	**Predicate:** K173536
Intended Use/Indications For Use	T2Candida 1.1 Panel and T2Dx Instrument is a qualitative T2 Magnetic Resonance (T2MR) assay for the direct detection of Candida species in K2EDTA human whole blood specimens from patients with symptoms of, or medical conditions predisposing the patient to, invasive fungal infections. The T2Candida 1.1 Panel identifies five species of Candida and categorizes them into the following three species groups: 1. Candida albicans and/or Candida tropicalis 2. Candida parapsilosis 3. Candida glabrata and/or Candida krusei The T2Candida 1.1 Panel does not distinguish between C. albicans and C. tropicalis. The T2Candida 1.1 Panel does not distinguish between C. glabrata and C. krusei. The T2Candida 1.1 Panel is indicated for the presumptive diagnosis of candidemia. The T2Candida 1.1 Panel is performed	Same

	independent of blood culture. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification. The T2Candida positive and negative External Controls (T2Candida QCheck Positive Kit and the T2Dx QCheck Negative Kit) are intended to be used as quality control samples with the T2Candida 1.1 Panel when run on the T2Dx Instrument. These controls are not intended for use with other assays or systems.	
Sample Type	Whole blood collected in a blood collection tube with EDTA anticoagulant	Same
Sample Volume	≥3 mL in a 4 mL K_2EDTA tube	Same
Test Platform	T2Dx Instrument	Same
Test Principle	Nucleic acid amplification followed by T2 magnetic resonance detection	Same
Test Cartridge	T2Candida test cartridge, sample inlet, and disposables	Same
Reagent Trays	T2Candida test reagents specific for the detection of *Candida*	Same
Targets	T2Candida Panel tests for five different species of *Candida* commonly associated with candidemia: *Candida albicans* and/or *Candida tropicalis, Candida parapsilosis, Candida glabrata* and/or *Candida krusei*	Same
General Device Characteristic Differences		
	Device: K234063	**Predicate:** K173536
Patient Population and Exclusions	Labeled for adult and pediatric patients (excluding neonates)	Labeled for adult patients

VI Standards/Guidance Documents Referenced:

ISO 15223-1 Fourth Edition 2021-07: Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements.

Premarket Assessment of Pediatric Medical Devices: Guidance for Industry and Food and Drug Administration Staff (March 24, 2014)

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

Most analytical performance metrics of the T2Candida 1.1 Panel were previously established in DEN140019 and K173536 and remain applicable under the expanded use with pediatric subjects. The sample matrix (human blood), device design, and sample workflow remain unchanged. In this submission, additional analytical studies were conducted as deemed necessary to ensure safety and effectiveness in this specific patient population. This approach is in accordance with the Premarket Assessment of Pediatric Medical Devices Guidance (2014).

1. Precision/Reproducibility:

   Device precision/reproducibility was assessed and deemed acceptable in DEN140019. Refer to the DEN140019 Decision Summary for additional details.

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Analytical Specificity

   Cross-reactivity was previously assessed with 80 non-target, clinically relevant or environmental organisms in DEN140019 and select species were found to be cross-reactive (see DEN140019 Decision Summary).

   Additional cross-reactivity testing was performed in this submission using five organisms clinically relevant to pediatric populations: *Streptococcus agalactiae, Listeria monocytogenes, Haemophilus influenzae, Streptococcus mitis,* and *Neisseria meningitidis.*

   Isolates were tested in triplicate at a concentration of 10^6 CFU/mL. Any organism that demonstrated cross-reactivity or gave an invalid result was further evaluated with additional replicates from two additional sample preparations at the same concentration and was tested at lower, more clinically relevant concentrations of organisms in blood (100-1000 CFU/mL).

   Cross-reactivity was defined as an increase in the T2 signal above the established cutoff for the *Candida* detection channel when tested at clinically relevant concentrations. Cross-reactivity required both amplification of the organism with the pan-*Candida* primers and subsequent detection with any of the capture probes. Of the five organisms tested, two demonstrated cross-reactivity at 10^6 CFU/mL (*S. agalactiae, H. influenzae*). Cross-reactivity was not observed when the organisms were re-tested at 1000 CFU/mL. The remaining three organisms did not demonstrate cross-reactivity (**Table 1**). The data are acceptable.

Table 1. T2Candida cross-reactivity results

Species	Concentration (CFU/mL)	Positive Results per Detection Panel			
		A/T	P	K/G	Internal Control
N. meningitidis	10^6 CFU/mL	0/3	0/3	0/3	Valid (3/3)

Species	Concentration (CFU/mL)	Positive Results per Detection Panel			
		A/T	P	K/G	Internal Control
S. mitis	10^6 CFU/mL	0/3	0/3	0/3	Valid (3/3)
L. monocytogenes	10^6 CFU/mL	0/3	0/3	0/3	Valid (3/3)
S. agalactiae	10^6 CFU/mL	0/3	0/3	1/3	Valid (3/3)
	10^6 CFU/mL*	0/6	0/6	1/6	Valid (6/6)
	1000 CFU/mL	0/3	0/3	0/3	Valid (3/3)
	100 CFU/mL	0/3	0/3	0/3	Valid (3/3)
	33 CFU/mL	0/3	0/3	0/3	Valid (3/3)
H. influenzae	10^6 CFU/mL	0/3	0/3	2/3	Valid (3/3)
	1000 CFU/mL	0/3	0/3	0/3	Valid (3/3)
	100 CFU/mL	0/3	0/3	1/3	Valid (3/3)
	100 CFU/mL *	0/6	0/6	0/6	Valid (6/6)
	33 CFU/mL	0/3	0/3	0/3	Valid (3/3)

A/T = *C. albicans/ C. tropicalis;* P = *C. parapsilosis;* K/G = *C. krusei / C. glabrata*

*For any cross-reactive result, two additional unique sample preparations were tested at the same concentration. Results were not considered cross-reactive if only one replicate demonstrated cross-reactivity.

Interference

An interference substances study was conducted as part of DEN140019. Results indicated interference with the signal for *Candida* species or with the signal for the internal control for the following substances: Feraheme, Magnevist, EDTA, Ablavar, and samples with an interferent simulating lipemia (Intralipid). Refer to the DEN140019 Decision Summary for additional information.

4. Assay Reportable Range:

Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Internal and external controls are unchanged in this submission and were previously validated in DEN140019. Refer to the DEN140019 Decision Summary for additional information.

Sample and reagent stability was previously validated in DEN140019 and K173536:

- Specimen stability at 2-8°C
- Lysis tube and reagent stability/shelf-life (12 months)
- Shipping stability

Use with pediatric populations will not alter the internal/external controls or stability. The data above are acceptable for the T2Candida 1.1 Panel.

6. Detection Limit:

The limit of detection for each *Candida* species was previously determined in DEN140019.

7. Assay Cut-Off:

Assay cut-off was previously established in DEN140019.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable. See Clinical Studies below.

2. Matrix Comparison:

   Not applicable.

C Clinical Studies:

Clinical study data from DEN140019 as well as additional data from studies that used the T2Candida 1.1 Panel with pediatric subjects were leveraged to support clinical performance of the device in subjects inclusive of adult and pediatric ages. This approach was based on the principles in the FDA Guidance, *Premarket Assessment of Pediatric Medical Devices*. As the course of the disease (invasive candidemia) is similar in adult and pediatric patients and the sample workflow and technological characteristics of the device remain unchanged, the amended labeling was supported by the existing clinical validation data conducted with adults.

The following principles were considered and deemed acceptably similar between the predicate device, as previously established for adult patients, and the subject device for a broader age-range subject population:

- Biological similarity of the sample (human whole blood)
- Biological similarity of disease in patient sub-populations
- No changes to device technology, design, reagents, or sample workflow

To further support testing in a pediatric population, data were evaluated from two studies from peer-reviewed literature in which the T2Candida 1.1 Panel was used to test samples from pediatric subjects. Detailed enrollment criteria, clinical protocols, patient demographic and clinical information, testing protocols, and detailed line data were provided for assessment. All samples were tested in accordance with the T2Candida 1.1 Panel instructions for use and compared to speciated *Candida* results from blood culture. A total of 246 samples were evaluated from patients aged <1 year to 17 years. Low prevalence (as determined by positive blood culture) was observed (1.2%). For all samples, estimates of sensitivity (PPA) ranged from 50-100% and specificity (NPA) ranged from 97-99%. The totality of data from pediatric and adult subjects support testing with the expanded patient age population.

1. Clinical Sensitivity:

   Clinical sensitivity was determined in DEN140019 using prospective and contrived samples. Refer to the DEN140019 Decision Summary.

2. Clinical Specificity:

Clinical sensitivity was determined in DEN140019 using prospective and contrived samples. Refer to the DEN140019 Decision Summary.

D Clinical Cut-Off:

The clinical cut-off was previously established in DEN140019.

E Expected Values/Reference Range:

The expected values/reference range were previously established in DEN140019.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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