SPECIAL 510(k): Device Modification
OIR Decision Summary

To: THE FILE **RE:** DOCUMENT NUMBER K173536

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II, Class III or Class I devices requiring 510(k). The following items are present and acceptable (delete/add items as necessary):

1. The name and 510(k) number of the SUBMITTER'S previously cleared device. (For a preamendments device, a statement to this effect has been provided.)

   Trade Name: T2Candida Panel and T2Dx Instrument
   DeNovo: DEN140019

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

   Submitter states in the submission that the intended use of the modified device has not changed from its predicate.

3. A description of the device **MODIFICATION(S),** including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**. **The modifications include the following**

   - Decreased cartridge stability (shelf life) was linked to the presence of two sealed post-testing decontamination bleach tubes. These bleach tubes have been removed from the T2Candida 1.1 Panel,
   - Modification of the T2Candida software to remove the bleach transfer steps from the T2Dx workflow,
   - Relabeling of the T2Candida External Positive and Negative Controls

4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including, labeling, intended use, physical characteristics, and software as shown in the table below.

Similarities		
Item	**Proposed Device: T2Candida 1.1 Panel (K173536)**	**Predicate Device: T2Candida Panel (DEN140019)**
Intended 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 T2Candida1.1 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 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.	T2Candida 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 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 Panel is indicated for the presumptive diagnosis of candidemia. The T2Candida Panel is performed independent of blood culture. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification.
Indication for Use	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.	The T2Candida Panel is indicated for the presumptive diagnosis of candidemia. The T2Candida Panel is performed independent of blood culture. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification.
Sample Type	4 ml whole blood collected in a blood collection tube with EDTA coagulant	Same
Test Platform	T2Dx	Same
Test Principle	PCR amplification followed by T2 patented medical resonance detection	Same
Throughput	Single cartridge test with random access with 7 draws on T2Dx	Same

Differences		
Item	**Proposed Device: T2Candida 1.1 Panel (K173536)**	**Predicate Device: T2Candida Panel (DEN140019)**
Device name	T2Candida Panel 1.1	T2Candida Panel
Test Cartridge Format	T2Candida 1.1 Panel Test Cartridge and disposables. No Bleach Tube – T2Candida 1.1 Panel Cartridge does not contain the two (2) bleach tubes or need for bleach transfer steps	T2Candida Panel Test Cartridge and disposables. Bleach Tubes included as part of cartridge and instructions enclosed
Cartridge stability (shelf life)	8 months	7 months
External Controls	The T2Candida positive and negative External Controls (T2Candida QCheck Positive and T2Dx QCheck Negative) 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.	The T2Candida positive and negative External Controls are intended to be used as quality control samples with the T2Candida Panel when run on the T2Dx Instrument. These controls are not intended for use with other assays or systems.
Software	Software v. 1.5.2.*XXXX* (*finalized build number pending*) is the upgrade to SW v.1.0.0.1031, eliminating workflow software commands for the final bleach transfer steps, prior to kit drawer ejection and disposal of assembled kit after test is completed.	Software v. 1.0.0.1031 includes bleach transfer steps performed prior to kit drawer ejection and disposal of assembled kit after test is completed.

The indications for use provided below are identical for both devices, except for renaming of the panel from T2Candida to T2Candida 1.1 and rebranding of the External Posive and Negative Controls.

Indications for use

The **T2Candida 1.1** Panel run on the T2Dx Instrument is a qualitative T2 Magnetic Resonance (T2MR) assay for the direct detection of Candida species in EDTA human whole blood specimens from patients with symptoms of, or medical conditions predisposing the patient to, invasive fungal infections. The T2Candida Panel identifies five species of Candida and categorizes them into the following three 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 Panel is indicated for the presumptive diagnosis of candidemia. The T2Candida panel is performed independent of blood cluture. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification.

The T2Candida positive (**T2Candida QCheck**) and negative External Controls (**T2Dx QCheck**) 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.

5. A **Design Control Activities Summary** which includes:

   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.

      A formal risk assessment was performed for the elimination of bleach tubes from the cartridge and impact on the T2Candida 1.1 Panel. The risk assessment performed utilized the T2Candida and T2Dx risk and hazard documentation including failure modes effects analyses (FMEAs), risk management reports and hazard assessment in order to review all content associated with the removal of the bleach tubes and cleanup step of the T2Dx system workflow. The risk analysis identified the following risks.

      1. Potential increase in false positive results due to contamination carryover of Candida spp. Amplicon external to the instrument from operator handling of consumables (touch-and-go contamination).
      2. Potential for incorrect operation of the instrument due to software changes to modify the T2Candida on-instrument assay workflow.

   b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied.

      The studies below were performed to demonstrate risk mitigation.

      Carryover and Cross-contamination study

      A carryover and cross-contamination study was conducted. Human whole blood pooled from healthy donors was triple-spiked with either 100 CFU/mL or 1000 CFU/mL of *C.albicans*, *C. parapsiolosis* and *C.glabrata* (APG) or *C. tropicalis*, *C. parapsilosis* and *C. krusei* (TPK). There were 49 APG (37 samples at 100 CFU/mL and 12 samples at 1000 CFU/mL) and 48 TPK (36 samples at 100 CFU/mL and 12 samples at 1000 CFU/mL) included in the study. One-hundred twenty nine (129) negative human whole blood samples were tested alongside the spiked, positive samples. Samples were loaded such that the Negative Samples and Positive APG or TPK samples were positioned in adjacent, alternating drawers. Two T2Candida 1.1 Panel cartridge lots and two reagent tray packs were and two T2Dx instruments were used in this study. Results were compared with the original data submitted to FDA (DEN140019) (**Table 1**). For all channels specificty was found to be $\geq$99%. These results support the risk assessment that removal of the bleach tubes results in similar assay specitificy as reported for the original cleared test.

Table 1. Results of Carry-Over and Cross-Contamination Studies for the Modified and Predicate Devices

Channel	T2Candida Panel %Specificity (95% CI)	T2Candida 1.1 Panel %Specificity (95% CI)
A/T	216/217 (99.5; 97.4-99.9)	128/128 (100; 97.1-100)
P	217/217 (100; 98.3-100)	127/128 (99.2; 95.7-99.9)
K/G	216/217 (99.5; 97.4-99.9)	127/128 (99.2; 95.7-99.9)
Overall	649/651 (99.7; 98.9-99.9)	382/384 (99.5; 98.1-99.9)

Cartridge Stability study

The T2Candida Panel cartridge was originally approved for use up to 8 months. However, decreased cartridge stability was identified by the sponsor and was attributed to corrosion of in-cartridge reagents, including those involved in PCR amplification. Thus, it was determined that bleach tubes, which only serve as a precautionary element of post-testing decontamination, should be removed from the cartridge. To assess the stability of the cartridge without bleach tubes, a real-time cartridge stability study was performed that measured T2MR signal at baseline (T=0), 1, 2, 3, 4, 6, 7, 8, and 9 months post-initiation. The study is also planned to continue to assess stability at 13 months post-initiation. Three (3) T2Candida 1.1 cartridge validation lots were tested during the course of the study, with two (2) lots stored at room temperature (15ºC-30ºC) and one lot stored in a controlled incubator at 30ºC. For each cartridge lot and time point eight (8) QCheck APG Positive External Controls and eight (8) T2Dx QCheck Negative External Control were evaluated. Cartridges were tested on multiple T2Dx instruments throughout the study. Stability acceptance criteria were as follows: For each time point tested for each lot, the A/T, P, and K/G channels of the T2Candida QCheck APG Positive control must be i) valid results with all channels POSITIVE and; ii) within a 45% negative drift in the differenceof mean T2MR values at T=0 baseline. Similiarly, all channels must be NEGATIVE (except for the Interal Control (IC)) for the T2Dx QCheck Negative control. Further, the IC channel of the T2Dx QCheck Negatives must also be within a 45% negative drift in the difference of mean T2MR values at T=0 baseline. The A/T, P, and K/G baseline levels in the T2Dx QCheck Negatives were also verified to be within a 45% positive drift in the difference of mean T2MR values determined at T=0. At present, all stability time points for the 3 catridge lots have passed all acceptance criteria out to 9 months, establishing stability for 8 months (**Table 2**). These results are acceptable.

Table 2. Summary of Cartridge Stability Testing to Date

Time point	Negative Sample Equivalence Test			Positive Sample Equivalence Test		
Cartridge Stability Lot	Lot 1 WO-05642	Lot 2 WO-05822	Lot 3 WO-05920	Lot 1 WO-05642	Lot 2 WO-05822	Lot 3 WO-05920
One Months (T1)	Pass	Pass	Pass	Pass	Pass	Pass
Two Months (T2)	Pass	Pass	Pass	Pass	Pass	Pass
Three Months (T3)	Pass	Pass	Pass	Pass	Pass	Pass
Four Months (T4)	Pass	Pass	Pass	Pass	Pass	Pass
Six Months (T6)	Pass	Pass	Pass	Pass	Pass	Pass
Seven Months (T7)	Pass	Pass	Pass	Pass	Pass	Pass
Eight Months (T8)	Pass	Pass	Pass	Pass	Pass	Pass
Nine Months (T9)	Pass	Pass	Pass	Pass	Pass	Pass

Software Modifications

Elimination of the the bleach steps required modifications to the T2Dx software v. 1.0.0.1031. The set of commands which executed the bleach transfer from the bleach tubes to all spent reaction wells in the cartridge assembly were eliminated for the T2Candida 1.1 Panel. The removed software commands do not interact with other steps in the workflow and are executed after results are reported; therefore, results reporting are not affected. All modifications are classified as low risk. These changes are acceptable.

Additionally, software updates have been made to the T2Dx platform that enhance the reliability of the platlform and to integrate T2Bacteria Panel Assay Definition Files into the overall menu. Included in these changes are modifications to results reporting. The original T2Candida Panel did not distinguish a potential assay error form an instrument error – all errors that led to no results reported were classified as “Invalid”. In the updated version (v. 1.5.2.XXX), potential assay errors due to low IC signal are returned as “Invalid” while other potential failures are reported as “Results Not Reported”. These changes are acceptable.

c) Declaration of Conformity to Design Controls

A "Declaration of Confromity" statement was submitted the T2 Biosystems, Inc. The statements are written below. Statement i and ii were signed by the Senior Director of Quality Management. The statements indicate that:

i. "To the best of my knowledge, the verification activities, as required by the risk analysis, for the modification were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met."
ii. The manufacturing facilty, T2 Biosystmes, Inc. is in conformance with the design control requirements as specified in 21 CFR 820.30 and the records are available for review."

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.