February 8, 2024

T2 Biosystems, Inc.
Rachel Gilbert
Manager, Regulatory Affairs
101 Hartwell Avenue
Lexington, Massachusetts 02421

Re: K233184
Trade/Device Name: T2Bacteria Panel
Regulation Number: 21 CFR 866.3960
Regulation Name: Nucleic Acid-Based Device For The Amplification, Detection, And Identification Of
Microbial Pathogens Directly From Whole Blood Specimens
Regulatory Class: Class II
Product Code: QBX, NSU
Dated: September 28, 2023
Received: September 28, 2023

Dear Rachel Gilbert:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above
and have determined the device is substantially equivalent (for the indications for use stated in the enclosure)
to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment
date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the
provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket
approval application (PMA). You may, therefore, market the device, subject to the general controls
provisions of the Act. Although this letter refers to your product as a device, please be aware that some
cleared products may instead be combination products. The 510(k) Premarket Notification Database
available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination
product submissions. The general controls provisions of the Act include requirements for annual registration,
listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and
adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We
remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be
subject to additional controls. Existing major regulations affecting your device can be found in the Code of
Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements
concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA
guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"
(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software
Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ribhi Shawar -S

Ribhi Shawar, Ph.D. (ABMM)
Branch Chief
General Bacteriology and Antimicrobial Susceptibility Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number *(if known)*
K233184

Device Name
T2Bacteria Panel

Indications for Use *(Describe)*

The T2Bacteria Panel run on the T2Dx Instrument is a qualitative T2 Magnetic Resonance (T2MR) test for the direct detection of bacterial species in K2EDTA human whole blood specimens from patients with suspected bacteremia. The T2Bacteria Panel identifies six species of bacteria: Acinetobacter baumannii, Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Staphylococcus aureus.

The T2Bacteria Panel is indicated as an aid in the diagnosis of bacteremia and results should be used in conjunction with other clinical and laboratory data. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification and for organisms not detected by the T2Bacteria Panel.

Results from the T2Bacteria Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions in patients with suspected bacteremia.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D)   ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary

Date of Summary February 5, 2024

Product Name T2Bacteria® Panel

Sponsor T2Biosystems, Inc.
101 Hartwell Avenue
Lexington, MA 02421

Correspondent Rachel Gilbert
Associate Director, Regulatory Affairs
781-226-2767, 1970
rgilbert@t2biosystems.com

Device Trade or Proprietary Name T2Bacteria® Panel

Regulation 21 CFR 866.3960

Common Name Nucleic acid-based device for the amplification, detection and identification of microbial pathogens directly from whole blood specimens

Product Code QBX, NSU

Classification Class II

The purpose of this pre-market 510(k) submission is to amend the T2Bacteria Panel initially cleared under K172708. The following changes to the Panel are addressed within the submission:

- Addition of *Acinetobacter baumannii* to the device intended use/indications for use

- Removal of the warnings related to false positives for *E. coli* and *P. aeruginosa* from the panel labeling

No changes have been made to the device components or technology since the initial clearance of the T2Bacteria Panel.

Intended Use

The T2Bacteria® Panel run on the T2Dx® Instrument is a qualitative T2 Magnetic Resonance (T2MR®) test for the direct detection of bacterial species in K_2EDTA human whole blood specimens from patients with suspected bacteremia. The T2Bacteria Panel identifies six species of bacteria: *Acinetobacter baumannii*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

The T2Bacteria Panel is indicated as an aid in the diagnosis of bacteremia and results should be used in conjunction with other clinical and laboratory data. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification and for organisms not detected by the T2Bacteria Panel.

Results from the T2Bacteria Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions in patients with suspected bacteremia.

Limitations

For prescription use only.

Please refer to the T2Bacteria Panel labeling for a more complete list of warnings, precautions, and contraindications.

Methodology

The T2Bacteria Panel detects and identifies six bacterial target species directly from whole blood specimens and independent of blood culture using nucleic acid amplification and proprietary T2MR detection technology. The assay is performed on the proprietary T2Dx platform. The whole blood specimen, drawn into a blood collection tube containing K_2EDTA is used for the test. The blood collection tube containing a minimum of 3 mL of blood is loaded directly onto the T2Dx instrument as part of the assembled Cartridge, a single use self-contained unit that contains all of the reagents and disposables required to run a single test. Fully automated on the T2Dx, the blood specimen is mixed with the Lysis Reagent to lyse the red blood cells and the bacterial cells are concentrated by centrifugation. The Internal Control is added to the concentrated bacterial cells, which then undergo a bead beating step to lyse the bacteria cells. The supernatant containing the DNA from the lysed bacterial cells and the Internal Control are amplified with the target and Internal Control specific primers. The generated amplicon is then aliquoted into individual tubes containing target specific conjugated particles for *Acinetobacter baumannii*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and the Internal Control. These individual tubes are read in the MR reader and a signal is generated.

Up to seven specimens can be loaded onto the T2Dx Instrument in parallel. When running a single specimen, the first result is reported in 3.5 hours from the time the specimen is loaded onto the instrument. The results are interpreted using the T2Dx applications software as valid or invalid, and if valid, target specific results are reported as Positive or Target not Detected. For one target, the *Escherichia coli* channel, results are reported as Positive, Indeterminate, or Target not Detected. An Indeterminate

result is a valid result, but the presence or absence of *Escherichia coli* cannot be definitively assessed, and the indeterminate status applies only to the *Escherichia coli* channel. Results are displayed on the T2Dx touchscreen and can be printed. Raw T2MR data are not available to the end user.

Summary of Analytical Performance (*Acinetobacter baumannii*)

Limit of Detection (LoD)

The limit of detection (LoD) for was determined by spiking whole blood specimens with *A. baumannii*. The LoD is defined as the lowest concentration (CFU/mL) of *A. baumannii*. that can be detected at a rate ≥ 95%. The LoD was established by testing a minimum of twenty replicates each of two strains of *A. baumannii*. at multiple concentrations. The LoD established for *A. baumannii*. in the T2Bacteria Panel is shown in Table 1.

Table 1: T2Bacteria Confirmed Limit of Detection – *Acinetobacter baumannii*

Species	Strain 1 LoD	Strain 2 LoD	Final Confirmed LoD
Acinetobacter baumannii	3 CFU/mL	3 CFU/mL	3 CFU/mL

Reproducibility

A multicenter reproducibility study was performed to determine the run to run, reagent lot, day to day and site to site reproducibility. Testing was performed at three sites (two external and one internal) with a panel of five target species, each tested in triplicate at two concentrations (1-2X LoD and 3-4X LoD) using two reagent lots. Testing was performed for six non-consecutive days with at least two operators per site for a total of 36 replicates per sample per site.

The reproducibility panel was comprised of each target species spiked in fresh human whole blood specimens in triple-spiked samples (*A. baumannii / K. pneumoniae / S. aureus* or *E. coli / P. aeruginosa / E. faecium*). Bacterial levels were confirmed by colony count testing of the original suspension used for spiking. A total of 108 negative blood samples were included in reproducibility panel.

Table 2: Summary of Reproducibility Results – *Acinetobacter baumannii*

Sample Type	Concentration		Ab
A.baumannii, S. aureus and *K. pneumoniae* Spike	1-2 x LoD	N Pos / N Total	108/108
		% Accurate	100
		95% CI	96.6-100
	3-4 x LoD	N Pos / N Total	108/108
		% Accurate	100
		95% CI	96.6-100
E. coli, P. aeruginosa, and *E. faecium* Spike	1-2 x LoD	N Pos / N Total	1/108
		% Accurate	99.1
		95% CI	94.9-100
	3-4 x LoD	N Pos / N Total	0/108
		% Accurate	100
		95% CI	96.6-100
Negatives	N/A	N Neg / N Total	108 / 108
		% Accurate	100
		95% CI	96.6-100

Analytical Reactivity (Inclusivity)

Analytical reactivity testing was conducted to ensure that the T2Bacteria Panel is capable of detecting multiple strains of *A. baumannii*. Clinical isolates were chosen based on resistance, phylogenetic, temporal, and geographic diversity and spiked into whole blood at 2-3x the established LoD.

A total of 14 organisms were evaluated for inclusivity of *A. baumannii* on the T2Bacteria Panel. Testing was performed in triplicate. In the event of a false negative result, testing was repeated with 20 replicates and 19/20 replicates had to generate a positive result to be considered passing. Test results summarized in Table 3 demonstrate that the T2Bacteria Panel is able to detect multiple strains of *A. baumannii*.

Table 3: Results Summary for T2Bacteria Reactivity (Inclusivity) Testing
– *Acinetobacter baumannii*

Isolate ID	N=3	N=20	Study Pass/Fail
17961	3/3	NT	Pass
BAA-2093	3/3	NT	Pass
BAA-1878	3/3	NT	Pass
BAA-747	2/3	20/20	Pass
BAA-1797	3/3	NT	Pass
51432	3/3	NT	Pass
17904	3/3	NT	Pass
BAA-1605	3/3	NT	Pass
13421	3/3	NT	Pass
LMG 10542	3/3	NT	Pass
LMG 10551	3/3	NT	Pass
LMG 1157	3/3	NT	Pass
LMG 22454	3/3	NT	Pass
CCUG 6644	3/3	NT	Pass

Analytical Specificity (Exclusivity)

Analytical exclusivity testing of the T2Bacteria Panel was conducted to assess the cross-reactivity of *A. baumannii* to non-panel species at 1,000 units/mL concentrations (CFU, $TCID_{50}$, or copies /mL where applicable) of pathogenically, phylogenetically, or environmentally relevant organisms in whole blood. Species that were shown to be potentially cross-reactive at the initial test concentration were further evaluated at lower target concentrations using a pre-defined titration scheme (100, 33, and 10 units/mL). Analytical testing of the T2Bacteria Panel included 128 different organisms comprised of the T2Bacteria Panel members themselves, viruses, and pathogenically, phylogenetically, or environmentally relevant bacterial and fungal species. The test results establish the specificity of *A. baumannii* on the T2Bacteria Panel in the presence of all organisms tested at 1,000 units / mL.

**Table 4: Bacteria Species for which no reactivity was detected at 1,000
CFU/mL – *Acinetobacter baumannii***

Non-Reactive Bacteria Species		
Acinetobacter calcoaceticus	*Escherichia fergusonii*	*Raoultella ornithinolytica*
Acinetobacter lwoffi	*Finegoldia magna*	*Raoultella planticola*
Acinetobacter nosocomialis	*Fusobacterium necrophorum*	*Salmonella enterica Enteritidis*
Acinetobacter pittii	*Fusobacterium nucleatum*	*Salmonella enterica Typhimurium*
Acinetobacter radioresistans	*Klebsiella oxytoca*	*Serratia marcescens*
Actinomyces israelii	*Klebsiella variicola*	*Shewanella putrefaciens*
Aeromonas hydrophila	*Lactobacillus acidophilus*	*Shigella boydii*
Bacteroides fragilis	*Lactococcus lactis*	*Shigella dysenteriae*
Burkholderia cepacia	*Leptotrichia trevisanii*	*Shigella flexneri*
Chryseobacterium indologenes	*Leuconostoc mesenteroides*	*Shigella sonnei*
Citrobacter koseri	*Listeria monocytogenes*	*Staphylococcus auricularis*
Clostridium sphenoides	*Moraxella catarrhalis*	*Staphylococcus capitis*
Corynebacterium jeikeium	*Morganella morganii*	*Staphylococcus epidermidis*
Cupriavidus pauculus	*Myroides odoratus*	*Staphylococcus haemolyticus*
Enterobacter aerogenes	*Ochrobactrum anthropi*	*Staphylococcus hominis*
Enterobacter cloacae	*Oligella urethralis*	*Staphylococcus lugdunensis*
Enterobacter hormaechei	*Pantoea agglomerans*	*Staphylococcus saprophyticus*
Enterococcus avium	*Parvimonas micra*	*Staphylococcus warneri*
Enterococcus caccae	*Pediococcus pentosaceus*	*Staphylococcus xylosus*
Enterococcus casseliflavus	*Peptostreptococcus anaerobius*	*Stenotrophomonas maltophilia*
Enterococcus cecorum	*Peptoniphilus harei*	*Streptococcus agalactiae*
Enterococcus dispar	*Plesiomonas shigelloides*	*Streptococcus anginosus*
Enterococcus durans	*Propionibacterium acnes*	*Streptococcus bovis*
Enterococcus faecalis	*Proteus mirabilis*	*Streptococcus constellatus*
Enterococcus gallinarum	*Proteus vulgaris*	*Streptococcus dysgalactiae*
Enterococcus gilvus	*Providencia stuartii*	*Streptococcus oralis*
Enterococcus hirae	*Pseudomonas alcaligenes*	*Streptococcus mutans*
Enterococcus italicus	*Pseudomonas fluorescens*	*Streptococcus pneumoniae*
Enterococcus malodoratus	*Pseudomonas luteola*	*Streptococcus pyogenes*
Enterococcus mundtii	*Pseudomonas oryzihabitans*	*Streptococcus salivarius*

Non-Reactive Bacteria Species		
Enterococcus pallens	*Pseudomonas pseudoalcaligenes (oleovorans)*	*Weeksella virosa*
Enterococcus pseudoavium	*Pseudomonas putida*	*Yersinia pseudotuberculosis*
Enterococcus raffinosus	*Pseudomonas stutzeri*	
Escherichia albertii	*Ralstonia pickettii*	

Table 5: Fungal Species for which no reactivity was detected at 1,000 CFU/mL – *Acinetobacter baumannii*

Non-Reactive Fungal Species		
Aspergillus fumigatus	*Candida parapsilosis*	*Fusarium oxysporum*
Aspergillus niger	*Candida tropicalis*	*Rhizomucor miehei*
Candida albicans	*Cryptococcus albidus*	*Rhizopus microsporus*
Candida glabrata	*Cryptococcus neoformans*	*Rhizopus oryzae*
Candida krusei	*Fusarium moniliforme*	*Rhodotorula glutinis*

Table 6: Viral Species for which no reactivity was detected at 1,000 units – *Acinetobacter baumannii*

Non-Reactive Viral Species		
Adenovirus[1]	Epstein-Barr Virus[2]	Herpes Simplex Virus 1[1]
Cytomegalovirus[1]	Hepatitis A Virus[2]	Herpes Simplex Virus 2[1]
Enterovirus Type 68[1]	Hepatitis B Virus[1]	Varicella-Zoster Virus[2]

[1]Units = $TCID_{50}$/mL; [2]Units= Copies/mL

Interfering Substances

Studies were conducted to evaluate the impact of potential endogenous and exogenous interfering substances on the performance of *A. baumannii* on the T2Bacteria Panel. These substances were added to negative whole blood samples or to whole blood samples multi-spiked with either *A. baumannii* at 2-3x LoD. Three replicate samples were run for each interfering substance tested.

All of the substances were tested in excess of standard reference or physiological levels and did not interfere with the performance of *A. baumannii* with the exception of Ferumoxytol (Feraheme). Initially, Ferumoxytol was tested at 618 μg/mL, which is threefold higher than its tmax of 206 μg/mL, but was found to be inhibitory to the performance of *A. baumannii* on the T2Bacteria Panel. Dilutions of Ferumoxytol

were performed and it was determined that concentrations ≥ 21 µg/mL interfere with the performance of *A. baumannii* on the T2Bacteria Panel.

Table 7: Substances Tested for Interference with the T2Bacteria Panel:
No Interference Observed – *Acinetobacter baumannii*

Endogenous Substances & Concentrations		Exogenous Substances & Concentrations			
Albumin	60 g/L	Amphotericin B Trihydrate	240 µg/mL	Gentamicin sulfate	21 µmol/L
ALT	120 U/liter	Ampicillin	152 µmol/L	Heparin	3,000 U/L
AST	144 U/liter	Azithromycin	15.3 µmol/L	Isovue 370	180 µL per 4mL vacutainer
Bilirubin (conjugated)	342 µmol/L	Caspofungin	52.8 µg/mL	Linezolid	55.8 µg/mL
Bilirubin (unconjugated)	342 µmol/L	Cefepime Hydrochloride	492 µg/mL	Lisinopril	0.74 µmol/L
Creatinine	50 mg/L	Cefazolin Sodium Salt	2.643 mmol/L	Magnevist (gadopentetate dimeglumine)	1.5 mM
Gamma Globulin	60 g/L	Cefoxitin Sodium Salt	180 µg/mL	Meropenem trihydrate	186 µg/mL
Hemoglobin	22.8 – 23.9 g/dL	Ceftazidime Pentahydrate	487 µg/mL	Metronidazole	701 µmol/L
Human DNA	2.2 µg/mL	Ciprofloxacin	30.2 µmol/L	Micafungin	90 mg/L
Intralipid (to mimic triglycerides)	3270 mg/dL	Clindamycin HCl	89.1 µmol/L	Piperacillin/Pipril	117 µg/mL
Lactoferrin	7.5 µmol/L	Cytarabine	32.4 µg/mL	Primaxin, 50:50 ratio of Imipenem: Cilastatin	528 µg/mL
Urea	42.9 mmol/L	Dexamethasone	1.53 µg/mL	Tazobactam (Tazobac)	18.9 µg/mL
White Blood Cells	2.08×10^7 - 2.48×10^7 cells/mL	EDTA	5.4 mg/mL	Vancomycin	103 µg/mL
		Fluconazole	245 µmol/L		

Competitive Inhibition

A Competitive Inhibition Study was conducted on the T2Bacteria Panel to evaluate *A. baumannii* performance in the presence of other Panel bacterial target species at high and low concentrations as well as selected bacterial and fungal non-Panel target organisms. The conditions tested included: co-infection with *A. baumannii* and an additional Panel target species both at or near the LoD; co-infection with *A. baumannii* and an additional Panel target species where one species is at high titer (1,000 CFU/mL) and the other is at or near the LoD; and co-infection with *A. baumannii* at or near the LoD and a non-Panel

species at high titer (1,000 CFU/mL). Four replicates were tested and if any false negative results were generated, the test was repeated with 20 replicates.

No competitive effects were observed in samples containing competing species at ≤1,000 CFU/mL for *A. baumannii* on the T2Bacteria Panel.

Summary of Clinical Performance (*Acinetobacter baumannii*)

The performance of *A. baumannii* on the T2Bacteria Panel was evaluated at eleven sites within the US and compared to the reference method of blood culture. Patients were enrolled prospectively and two paired sample collections, one for blood culture and one for testing by the T2Bacteria Panel were drawn from each subject. The blood culture systems used in the study were BD Bactec™ FX, bioMerieux BacT/ALERT™, and Thermo Fisher VersaTREK®. Species identification was performed on all positive bacteria cultures and methods included Gram stain, bioMerieux Vitek® 2, bioMerieux or Bruker MALDI TOF, and PCR. The T2Bacteria Panel *A. baumannii* result was compared against results from these blood culture systems for Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA). A total of 1,427 subjects were tested prospectively. Due to the low prevalence of the organisms contained in the Panel, an additional 50 contrived specimens were evaluated at three sites. Contrived specimens were prepared by spiking *A. baumannii* at defined concentrations (CFU/mL) into healthy donor whole blood. Further, an additional 300 blood samples not spiked with *A. baumannii* members were also evaluated as part of the contrived arm of the study. 250 of these blood samples were spiked with the additional 5 bacterial species available on the T2Bacteria Panel (50 each).

Table 8 summarizes the overall PPA (sensitivity) and NPA (specificity) of *A. baumannii* from the prospective and contrived arms of the study.

Table 8: Overall Performance of the T2Bacteria Panel in the Clinical Study – *Acinetobacter baumannii*

Species	Sensitivity (PPA)		Specificity (NPA)	
	PPA (TP / (TP + FN))	95% CI	NPA (TN / (FP + TN))	95% CI
A. baumannii	97.5% (39/40)	87.1% - 99.6%	99.2% (1713/1727)	98.6% - 99.5%

- Sensitivity (PPA) calculated against samples with titer levels at or above limit of detection (LoD) in Contrived Arm and blood culture positives in Prospective Arm

- Specificity (NPA) calculated from all samples (including below LoD and unspiked negative samples) as the total number of negative channels divided by total number of non-spiked channels in Contrived Arm and blood culture negatives in Prospective Arm.

Prospective Arm: T2Bacteria Panel Performance vs. Blood Culture

In the prospective arm of the study, the specificity (NPA) of *A. baumannii* on the T2Bacteria Panel against blood culture from all included subjects was evaluated. The sensitivity (PPA) could not be calculated for *A. baumannii* as there were no positive specimens identified by blood culture.

**Table 9: T2Bacteria Panel Performance Characteristics for the
Prospective Arm of the Clinical Study – *Acinetobacter baumannii***

| Target Species | PPA | | NPA | |
	Sensitivity	95% CI	Specificity	95% CI
A. baumannii	--- (0/0)	---	99.1% (1414/1427)	98.4 - 99.5%

**Table 10: T2Bacteria Panel vs. Blood Culture Contingency table, All
Included Subjects – *Acinetobacter baumannii***

Ab			
		Blood culture	
		+	-	
T2	+	0	13	13
	-	0	1414	1414
		0	1427	1427

	Value	- 95% CI	+ 95% CI
PPA	---	---	---
NPA	99.1%	98.4%	99.5%

Contrived Arm

Results for the Contrived arm were further analyzed based on *A. baumannii* concentration (either above or below the LoD).

**Table 11: PPA for Contrived Specimens Above and Below the LoD –
*Acinetobacter baumannii***

| Target Species | LoD (CFU/mL) | ≥ LoD | | < LoD | |
		PPA	95% CI	PPA	95% CI
A. baumannii	3	97.5% (39/40)	87.1 - 99.6%	40.0% (4/10)	16.8 - 68.7%

Evaluation of False Positive Results

Overall, in the prospective study, there were 13 T2+/BC- potential false positive *A. baumannii* positive results. consisting of 35 T2+/BC+ concordant results and 155 T2+/BC- potential false positive results. Of the 13 potential false positive results, 1 represented a result for which an additional blood specimen (drawn at the same time as the original positive T2 specimen) was positive by an amplification and gene sequencing method.

Table 12: Summary of T2 (+)/BC (-) Results in Prospective Arm –
Acinetobacter baumannii

Species	T2(+) / BC(-) total	Other Blood Culture positive[1]	Sequencing positive[2]	T2(+) / BC(-) associated with strong evidence of infection[3]	T2(+) / BC(-) associated with other evidence of infection Non-Blood Matrices Culture Positive[4]	T2(+) / BC(-) associated with no evidence of infection
A. baumannii	13	0	1	7.7% (1/13)	0.0% (0/13)	92.3 %(12/13)

[1] Blood cultures positive for the T2 species identified other than the paired blood culture and processed within ± 14 days of collection of the T2 sample.

[2] Sequencing from blood samples drawn at the same time as collection of the T2 sample and positive for the T2 species identified, where this sequencing assay was only run on subjects without positive evidence from other sample sources (footnote 1 and 4).

[3] Strong evidence defined as a T2 positive result associated with a blood culture positive from a different draw than T2 draw or a sequencing positive result from a blood sample drawn concurrently with the T2 draw.

Evaluation of *A. baumannii, E. coli,* and *P. aeruginosa* Detection in Negative Blood Samples

Following manufacturing process and facility improvements undertaken by T2 Biosystems to improve the cleanliness of the reagents in the T2Bacteria Panel, data from the testing for ten (10) different lots of T2Bacteria Panel reagents with negative human whole blood was retrospectively pulled and evaluated for percent false positivity. A total of 980 valid samples were evaluated, 98 replicates for each reagent lot. Testing demonstrated *A. baumannii* had an overall fall positive percentage of 0.2%, *E. coli* had an overall false positive percentage of 0.5%, and *P. aeruginosa* had an overall false positive percentage of 0.4%.

A. baumannii

Testing negative whole blood with ten different lots of T2Bacteria Panel reagents resulted in two (2) lots that contained a single *A. baumannii* false positive each. Across the different lots the NPA ranged from 99% to 100%. Overall results from testing 980 samples demonstrated a 99.8% NPA and a false positive percentage of 0.2%.

E. coli

Testing negative whole blood with ten different lots of T2Bacteria Panel reagents resulted in single false positive detection of *E. coli* in 5 different lots. Across the different lots the NPA ranged from 99% to 100%. Overall results from testing 980 samples demonstrated a 99.5% NPA and a false positive percentage of 0.5%.

P. aeruginosa

Testing negative whole blood with ten different lots of T2Bacteria Panel reagents resulted in three (3) lots that contained false positives for *P. aeruginosa*. Across the different lots the NPA ranged from 98% to 100%. Overall results from testing 980 samples demonstrated a 99.6% NPA and a false positive percentage of 0.4%.

Table 13: Percent False Positive – *A. baumannii, E. coli, P. aeruginosa*

Channel	% False Positive	95% CI
A. baumannii	0.2%	0.1% - 0.7%
E. coli	0.5%	0.2% - 1.2%
P. aeruginosa	0.4%	0.2% - 0.4%

Additional Testing of *A. baumannii* Contrived Samples

Testing was completed on thirty-three unique strains of *Acinetobacter baumannii* that were spiked individually into human whole blood at 2-3x LoD (6-9 CFU/mL). Testing was conducted across four (4) different T2Dx devices, utilized two (2) lots of cartridges, two (2) lots of reagents and blood from five (5) unique donors over 9 testing days. Testing demonstrated positive detection of all strains except for one (32/33).

Table 14: PPA for *A. baumannii*

A. baumannii Concentration Tested	PPA (TP/(TP+FN))	95% CI
6-9 CFU/mL	97.0% (32/33)	84.7 – 99.5%

Predicate Comparison

Table 15: Comparison Between T2Bacteria Panel and Predicate Device

Characteristic	T2Bacteria Panel (New Device)	T2Bacteria Panel (K172708) (Predicate Device)
Similarities		
FDA Product Code	QBX, NSU	Same
Regulatory Classification	Class II	Same
Regulation Number	21 CFR 866.3960	Same
Intended Use/Indications for Use	The T2Bacteria Panel run on the T2Dx® Instrument is a qualitative T2 magnetic resonance (T2MR®) test for the direct detection of bacterial species in K_2EDTA human whole blood specimens from patients with suspected bacteremia. The T2Bacteria Panel identifies six species of bacteria: *Acinetobacter baumannii, Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Staphylococcus aureus*. The T2Bacteria Panel is indicated as an aid in the diagnosis of bacteremia and results should be used in conjunction with other clinical and laboratory data. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification and for organisms not detected by the T2Bacteria Panel. Results from the T2Bacteria Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions in patients with suspected bacteremia.	The T2Bacteria Panel run on the T2Dx® Instrument is a qualitative T2 magnetic resonance (T2MR®) test for the direct detection of bacterial species in K_2EDTA human whole blood specimens from patients with suspected bacteremia. The T2Bacteria Panel identifies five species of bacteria: *Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Staphylococcus aureus*. The T2Bacteria Panel is indicated as an aid in the diagnosis of bacteremia and results should be used in conjunction with other clinical and laboratory data. Concomitant blood cultures are necessary to recover organisms for susceptibility testing or further identification and for organisms not detected by the T2Bacteria Panel. Results from the T2Bacteria Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions in patients with suspected bacteremia.
Sample Type	4 ml whole blood collected in a blood collection tube with K_2EDTA anticoagulant	Same
Test Platform	T2Dx Instrument	Same
Reagent Trays	T2Bacteria Test Reagents for detection of bacteria	Same
Test Cartridge Format	T2Bacteria Test Cartridge and disposables	Same
Test Principle	Nucleic acid amplification followed by T2 magnetic resonance detection	Same

Differences		
Characteristic	**T2Bacteria Panel (New Device)**	**T2Bacteria Panel (K172708) (Predicate Device)**
Targets	Six (6) different species of bacteria commonly implicated in bacteremia: *Acinetobacter baumannii, Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Staphylococcus aureus*	Five (5) different species of bacteria commonly implicated in bacteremia: *Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Staphylococcus aureus*
Warnings Statements – False-Positives	None	During prospective clinical studies, false positive results were observed for *E. coli* and *P. aeruginosa* in prospectively collected specimens. Users should be aware of the possibility of occurrence of false positive results, especially for *E. coli* and *P. aeruginosa* and should closely monitor QCheck negative control results for any trends and determine the need for action.