May 24, 2018

T2 Biosystems, Inc.
Tom Lowery
Chief Operations Officer
101 Hartwell Avenue
Lexington, Massachusetts 02421

Re: K172708
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: April 30, 2018
Received: May 1, 2018

Dear Tom Lowery:

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 (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. 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.

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 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR

Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/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 For

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K172708

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 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.

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.

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15. 510(k) SUMMARY

Date of Summary	April 30, 2018
Product Name	T2Bacteria® Panel
Sponsor	T2 Biosystems, Inc. 101 Hartwell Avenue Lexington, MA 02421
Correspondent	T2 Biosystems, Inc. Thomas J. Lowery, PhD Chief Scientific Officer Office Phone : (781) 457-1223 Mobile Phone : (617) 932-9047 Fax : (781) 357-3080 tlowery@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

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Substantial Equivalence

COMPARISON OF NEW DEVICE WITH PREDICATE DEVICE

Characteristic	**T2Bacteria Panel** (New Device)	**T2Candida Panel (DN 140019)** (Primary Predicate Device)
Similarities		
FDA Product Code	QBX, NSU	PII, NSU
Regulatory Classification	Class II	Class II
Regulation Number	21 CFR 866.3960	21 CFR 866.3960
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 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.	T2Candida 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 Panel identifies five species of Candida and categorizes them into the following three (3) 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. 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.
Sample Type	4 ml whole blood collected in a blood collection tube with K_2EDTA anticoagulant	4 ml whole blood collected in a blood collection tube with K_2EDTA anticoagulant
Test Platform	T2Dx	T2Dx
Test Cartridge Format	T2Bacteria Test Cartridge and disposables	T2Candida test cartridge and disposables
Test Principle	Nucleic acid amplification followed by T2 magnetic resonance detection	Nucleic acid amplification followed by T2 magnetic resonance detection
Through put	Single cartridge test with random access with seven (7) draws on T2Dx	Single cartridge test with random access with seven (7) draws on T2Dx
Differences		

Characteristic	**T2Bacteria Panel** (New Device)	**T2Candida Panel (DN 140019)** (Primary Predicate Device)
Reagent Trays	T2Bacteria Test Reagents for detection of bacteria	T2Candida test reagent for detection of Candida (difference is specific to primers and probes)
Targets	T2Bacteria Panel tests for five (5) different species of bacteria commonly implicated in bacteremia: *Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Staphylococcus aureus.*	T2Candida Panel tests for five (5) different species of Candida commonly associated with candidemia: *Candida albicans and/or Candida tropicalis; Candida parapsilosis; Candida glabrata and/or Candida krusei*

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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 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.

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 five 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 *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.

Performance Data

For ease of reference, Table 1 defines the target organisms contained in the T2Bacteria Panel and common acronyms used in the study descriptions and tables.

Table 1: T2Bacteria Assay Targets	
Organism	**Acronym**
Enterococcus faecium	Efm
Escherichia coli	Eci
Klebsiella pneumoniae	Kp
Pseudomonas aeruginosa	Pa
Staphylococcus aureus	Sa
Internal Control	IC

i. Limit of Detection (LoD)

The limit of detection (LoD) for each bacterial species was determined by spiking whole blood specimens with each individual bacteria target species. For each bacterial target, the LoD is defined as the lowest concentration (CFU/mL) of target that can be detected at a rate ≥ 95%. The LoD was established by testing a minimum of twenty replicates each of two strains of each bacteria species at multiple concentrations. The LoD established for each bacteria in the T2Bacteria Panel is shown in Table 2a.

Table 2a: T2Bacteria Panel LoD	
Bacteria	**LoD (CFU/mL)**
Enterococcus faecium	5
Escherichia coli	11
Klebsiella pneumoniae	2
Pseudomonas aeruginosa	5
Staphylococcus aureus	2

ii. Reproducibility

To confirm the site-to-site, operator-to-operator, system-to-system, and lot-to-lot reproducibility of the T2Bacteria Panel, negative blood and blood spiked with Kp and Sa or Efm, Pa, and Eci were tested at 1-2x LoD and 3-4x LoD at three sites, with three to four operators per site, two lots of reagents, and three T2Dx systems. Each sample type in the study was tested over six non-consecutive days. A total of 540 samples comprised of 108 negative samples and 432 positive samples were run with an overall reproducibility of 98.7%. The data, summarized in Tables 2b and 2c demonstrate that the T2Bacteria Panel run on the T2Dx across sites, operators, reagent lots, and systems performs reproducibly.

Table 2b: T2Bacteria Panel Reproducibility – Overall Performance

Sample	N Accurate / N Total	% Accurate	95% CI
Total	533/540	98.7	97.3-99.5

Table 2c: T2Bacteria Panel Reproducibility

		Eci	Efm	Kp	Pa	Sa
KS 1-2x LoD	N Pos / N Total	5/108	0/108	108/108	0/108	105/108
	% Accurate	95.4	100	100	100	97.2
	95% CI	89.5-98.5	96.6-100	96.6-100	96.6-100	92.1-99.4
KS 3-4x LoD	N Pos / N Total	5/108	0/108	108/108	1/108	108/108
	% Accurate	95.4	100	100	99.1	100
	95% CI	89.5-98.5	96.6-100	96.6-100	94.9-100	96.6-100
EPE 1-2x LoD	N Pos / N Total	108/108	107/108	0/108	108/108	0/108
	% Accurate	100	99.1	100	100	100
	95% CI	96.6-100	94.9-100	96.6-100	96.6-100	96.6-100
EPE 3-4x LoD	N Pos / N Total	108/108	108/108	0/108	108/108	0/108
	% Accurate	100	100	100	100	100
	95% CI	96.6-100	96.6-100	96.6-100	96.6-100	96.6-100
Neg	N Neg / N Total	106 / 108	108 / 108	108 / 108	107/108	108 / 108
	% Accurate	98.1	100	100	99.1	100
	95% CI	93.5-99.8	96.6-100	96.6-100	94.9-100	96.6-100

iii. Analytical Reactivity (Inclusivity):

Analytical reactivity testing was conducted to ensure that the T2Bacteria Panel is capable of detecting multiple strains of the five organisms that constitute the panel. Clinical isolates were chosen based on resistance, phylogenetic, temporal, and geographic diversity and spiked into whole blood at 2-3x the established panel LoDs. Inclusivity panels included the following:

- 11 *Enterococcus faecium* strains
- 12 *Escherichia coli* strains
- 13 *Klebsiella pneumonia* strains
- 13 *Pseudomonas aeruginosa* strains
- 8 *Staphylococcus aureus* strains

A total of 57 organisms were evaluated for inclusivity in 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 each target species.

Table 3: T2Bacteria Panel Inclusivity Results

Species	Isolate ID	N=3	N=20
Enterococcus faecium	ATCC BAA-472	3/3	NT
Enterococcus faecium	ATCC 51559	3/3	NT
Enterococcus faecium	ATCC 49224	3/3	NT
Enterococcus faecium	ATCC 700221	3/3	NT
Enterococcus faecium	ATCC BAA-2320	3/3	NT
Enterococcus faecium	ATCC 51858	3/3	NT
Enterococcus faecium	DSM 17050	3/3	NT
Enterococcus faecium	LMG 16308	3/3	NT
Enterococcus faecium	LMG 20732	3/3	NT
Enterococcus faecium	LMG 23226	3/3	NT
Enterococcus faecium	LMG 24170	3/3	NT
Escherichia coli	ATCC 31705	3/3	NT
Escherichia coli	ATCC BAA-2326	3/3	NT
Escherichia coli	ATCC 700928	3/3	NT
Escherichia coli	ATCC BAA-2452	3/3	NT
Escherichia coli	ATCC BAA-1652	3/3	NT
Escherichia coli	ATCC BAA-2129	3/3	NT
Escherichia coli	ATCC 35150	3/3	NT
Escherichia coli	ATCC 23518	3/3	NT
Escherichia coli	ATCC 29640	3/3	NT
Escherichia coli	ATCC BAA-177	3/3	NT
Escherichia coli	ATCC 33780	3/3	NT
Escherichia coli	ATCC BAA-179	3/3	NT
Klebsiella pneumoniae	ATCC 27736	3/3	NT
Klebsiella pneumoniae	ATCC 6908	3/3	NT
Klebsiella pneumoniae	ATCC BAA-1144	3/3	NT
Klebsiella pneumoniae	ATCC 29013	3/3	NT
Klebsiella pneumoniae	ATCC BAA-1898	3/3	NT
Klebsiella pneumoniae	ATCC BAA-1903	3/3	NT
Klebsiella pneumoniae	ATCC BAA-1904	3/3	NT
Klebsiella pneumoniae	ATCC 13884	2/3	20/20
Klebsiella pneumoniae	ATCC 13886	3/3	NT
Klebsiella pneumoniae	ATCC 8045	3/3	NT
Klebsiella pneumoniae	CCUG 26108	3/3	NT
Klebsiella pneumoniae	ATCC BAA-2578	3/3	NT
Klebsiella pneumoniae	ATCC 700603	2/3	20/20
Pseudomonas aeruginosa	ATCC 47085	3/3	NT
Pseudomonas aeruginosa	ATCC 43637	3/3	NT

Table 3: T2Bacteria Panel Inclusivity Results			
Species	**Isolate ID**	**N=3**	**N=20**
Pseudomonas aeruginosa	ATCC 14203	3/3	NT
Pseudomonas aeruginosa	ATCC 15692	3/3	NT
Pseudomonas aeruginosa	LMG 25200	3/3	NT
Pseudomonas aeruginosa	LMG 27623	3/3	NT
Pseudomonas aeruginosa	ATCC 27853	3/3	NT
Pseudomonas aeruginosa	LMG 24907	3/3	NT
Pseudomonas aeruginosa	LMG 24916	3/3	NT
Pseudomonas aeruginosa	LMG 24918	3/3	NT
Pseudomonas aeruginosa	LMG 24928	3/3	NT
Pseudomonas aeruginosa	LMG 25009	3/3	NT
Pseudomonas aeruginosa	LMG 25143	3/3	NT
Staphylococcus aureus	ATCC 33592	2/3	19/20
Staphylococcus aureus	ATCC BAA-1556	3/3	NT
Staphylococcus aureus	ATCC BAA-42	3/3	NT
Staphylococcus aureus	ATCC BAA-1717	3/3	NT
Staphylococcus aureus	ATCC 11371	3/3	NT
Staphylococcus aureus	ATCC 12598	3/3	NT
Staphylococcus aureus	ATCC BAA-44	3/3	NT
Staphylococcus aureus	ATCC BAA-1683	3/3	NT

NT: Not tested

iv. Analytical Exclusivity

Analytical exclusivity testing of the T2Bacteria Panel was conducted to assess the cross-reactivity of the T2Bacteria Panel 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, summarized in Tables 4a and 4b, establish the specificity of the T2Bacteria Panel in the presence of all organisms tested at 1,000 units / mL with the exception of *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Enterococcus durans*, *Escherichia albertii*, *Escherichia fergusonii*, and *Klebsiella variicola* for which cross-reactivity was established at titer levels ≤ 10 units/mL.

Table 4a: T2Bacteria Panel Exclusivity Results					
Organisms With No Reactivity at 1000 units/mL (CFU/mL, TCID50/mL, copies/mL as applicable)					
Fungi					
Aspergillus fumigatus	*Aspergillus niger*	*Candida albicans*	*Candida glabrata*	*Candida krusei*	*Candida parapsilosis*
Candida tropicalis	*Cryptococcus albidus*	*Cryptococcus neoformans*	*Fusarium moniliforme*	*Fusarium oxysporum*	*Rhizomucor meihei*
Rhizopus microsporus		*Rhizopus oryzae*		*Rhodotorula glutinis*	
Viruses					
Adenovirus type 1	Cytomegalovirus	Epstein-Barr Virus	Hepatitis A Virus	Hepatitis B Virus	
Herpes Simplex Virus 1		Herpes Simplex Virus 2		Varicella Zoster Virus	
Gram Positive Bacteria					
Actinomyces israelii	Clostridium sphenoides	*Corynebacterium jeikeium*	*Enterococcus avium*	*Enterococcus caccae*	*Enterococcus casseliflavus*
Enterococcus cecorum	*Enterococcus dispar*	*Enterococcus faecalis*	*Enterococcus gallinarum*	*Enterococcus gilvus*	*Enterococcus hirae*
Enterococcus italicus	*Enterococcus malodoratus*	*Enterococcus mundtii*	*Enterococcus pallens*	*Enterococcus pseudoavium*	*Enterococcus raffinosus*
Finegoldia magna	*Lactobacillus acidophilus*	*Lactococcus lactis*	*Leuconostoc mesenteroides*	*Listeria monocytogenes*	*Parvimonas micra*
Pediococcus pentosaceus	*Peptoniphilus harei*	*Peptostreptococcus anaerobius*	*Propionibacterium acnes*	*Staphylococcus auricularis*	*Staphylococcus capitis*
Staphylococcus epidermidis	*Staphylococcus haemolyticus*	*Staphylococcus hominis*	*Staphylococcus lugdunensis*	*Staphylococcus saprophyticus*	*Staphylococcus warneri*
Staphylococcus xylosus	*Streptococcus agalactiae*	*Streptococcus anginosus*	*Streptococcus bovis*	*Streptococcus constellatus*	*Streptococcus dysgalactiae*
Streptococcus mutans	*Streptococcus pneumoniae*	*Streptococcus pyogenes*	*Streptococcus salivarius*	*Streptococcus oralis*	
Gram Negative Bacteria					
Acinetobacter calcoaceticus	*Acinetobacter lwoffi*	*Acinetobacter nosocomialis*	*Acinetobacter pittii*	*Acinetobacter radioresistans*	*Aeromonas hydrophila*
Bacteroides fragilis	*Burkholderia cepacia*	*Chryseobacterium indologenes*	*Citrobacter koseri*	*Cupriavidus pauculus*	
Enterobacter aerogenes	*Enterobacter cloacae*	*Enterobacter hormaechei*	*Fusobacterium necrophorum*	*Fusobacterium nucleatum*	*Klebsiella oxytoca*
Leptotrichia trevisanii	*Moraxella catarrhalis*	*Morganella morganii*	*Myroides odoratus*	*Ochrobactrum anthropi*	*Oligella urethralis*
Pantoea agglomerans	*Plesiomonas shigelloides*	*Proteus mirabilis*	*Proteus vulgaris*	*Providencia stuartii*	*Pseudomonas alcaligenes*
Pseudomonas fluorescens	*Pseudomonas luteola*	*Pseudomonas oryzihabitans*	*Pseudomonas pseudoalcaligenes (oleovorans)*		*Pseudomonas putida*
Pseudomonas stutzeri	*Ralstonia pickettii*	*Raoultella ornithinolytica*	*Raoultella planticola*	*Salmonella enterica Enteritidis*	
Salmonella enterica Typhimurium	*Serratia marcescens*	*Shewanella putrefaciens*	*Stenotrophomonas maltophilia*	*Weeksella virosa*	
Yersinia pseudotuberculosis					

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Table 4b: T2Bacteria Panel Exclusivity Results	
Organisms That React at ≤ 10 units/mL (CFU/mL)	
Cross Reactive Species	**Cross Reacts with T2Bacteria Channel**
Enterococcus durans	*E. faecium*
Escherichia albertii	*E. coli*
Escherichia fergusonii	*E. coli*
Klebsiella variicola	*K. pneumoniae*
Shigella boydii	*E. coli*
Shigella dysenteriae	*E. coli*
Shigella flexneri	*E. coli*
Shigella sonnei	*E. coli*

Based on *in silico* analysis, *Yersinia pestis* is not expected to cross-react with any T2Bacteria channel. *In silico* analysis also showed that the new species *Klebsiella quasipneumoniae*, which was recently reclassified from *K. pneumoniae* phylogroup KpII to *Klebsiella quasipneumoniae*, is expected to cross-react with the *K. pneumoniae* T2Bacteria channel. Similarly, the new species *Staphylococcus argenteus*, which was recently reclassified from *S. aureus* clonal complex 75 to *Staphylococcus argenteus*, is expected to cross-react with *S. aureus* T2Bacteria channel. These organisms have not been tested.

For one species, Enterovirus Type 68, 0 of 3 replicates tested at 1,000 $\mathrm{TCID_{50}/mL}$ were positive for *E. coli*; 1 of 6 replicates tested at 316 $\mathrm{TCID_{50}}$/mL were positive on the *E. coli* channel of the Panel. This species was deemed not cross reactive.

v. Competitive Inhibition

T2 Biosystems conducted a Competitive Inhibition Study on the T2Bacteria Panel to evaluate assay performance in the presence of two or more 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 two Panel target species both at or near the LoD; co-infection with two 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 one Panel species 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. If a ≤95% hit rate in the 20 replicates was generated, the concentration of the competing organism was titrated to determine the level at which the reaction is not inhibited.

Results from combinations of Panel members at or near the LoD tested when co-infected with a competing Panel member at either 1,000 CFU/mL or also at or near the LoD are shown in Table 5a. False negative results were repeated with 20 replicates and all had 100% hit rates with the exception of the co-infection of *P. aeruginosa* (at or near the LoD) and *E. coli* (1,000 CFU/mL). For this combination, detection of *P. ae*ruginosa had a hit rate of

18/20. When *E. coli* concentrations were reduced to 100, 33, and 10 CFU/mL, *P. aeruginosa* at or near the LoD was detected at a rate of 100%.

Results from combinations of Panel members at or near the LoD tested when co-infected with other clinically relevant organisms at 1,000 CFU/mL are shown in Table 5b. False negative results were repeated with 20 replicates and all had 100% hit rate.

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Table 5a: T2Bacteria Panel Competitive Inhibition Results (Positivity) Co-infection with Two T2Bacteria Panel Members

	Efm (5-10 CFU/mL)		**Eci (11-22 CFU/mL)**		**Kp (2-4 CFU/mL)**		**Pa (5-10 CFU/mL)**		**Sa (2-4 CFU/mL)**	
Competing	**Efm**	**Comp. Org.**	**Eci**	**Comp. Org.**	**Kp**	**Comp. Org.**	**Pa**	**Comp. Org.**	**Sa**	**Comp. Org.**
Efm (5-10 CFU/mL)	N/A		4/4	4/4	4/4	4/4	4/4	4/4	4/4	4/4
Efm (1,000 CFU/mL)			4/4	4/4	4/4	4/4	4/4	4/4	4/4	4/4
Eci (11-22 CFU/mL)	4/4	4/4	N/A		4/4	4/4	2/4*	4/4	4/4	4/4
Eci (1,000 CFU/mL)	4/4	4/4			4/4	4/4	2/4*	4/4	4/4	4/4
Kp (2-4 CFU/mL)	4/4	4/4	4/4	4/4	N/A		4/4	4/4	4/4	4/4
Kp (1,000 CFU/mL)	4/4	4/4	4/4	4/4			4/4	4/4	4/4	4/4
Pa (5-10 CFU/mL)	4/4	4/4	4/4	4/4	4/4	4/4	N/A		4/4	4/4
Pa (1,000 CFU/mL)	4/4	4/4	3/4*	4/4	4/4	4/4			4/4	4/4
Sa (2-4 CFU/mL)	4/4	4/4	4/4	4/4	4/4	4/4	4/4	3/4*	N/A	
Sa (1,000 CFU/mL)	4/4	4/4	4/4	4/4	4/4	4/4	4/4	4/4		

*Required repeat testing at N=20; all yielded 20/20 hit rates except Pa (5-10 CFU/mL) with Eci (1,000 CFU/mL).

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Table 5b: T2Bacteria Panel Competitive Inhibition Results Co-infection with Organisms Other than T2Bacteria Panel Members						
Competing Organism	**Test Concentration (CFU/mL)**	**T2Bacteria Panel Members (Hit Rate)**				
		Efm (5-10 CFU/mL)	**Eci (11-22 CFU/mL)**	**Kp (2-4 CFU/mL)**	**Pa (5-10 CFU/mL)**	**Sa (2-4 CFU/mL)**
S. epidermidis	1000	4/4	4/4	4/4	4/4	4/4
S. haemolyticus	1000	4/4	4/4	4/4	4/4	4/4
S. pneumoniae	1000	4/4	4/4	4/4	3/4*	4/4
E. cloacae	1000	4/4	4/4	4/4	4/4	4/4
S. salivarius	1000	4/4	4/4	4/4	4/4	4/4
C. albicans	1000	4/4	4/4	4/4	4/4	4/4

* Required repeat testing and yielded 20/20 hit rate.

vi. Interfering Substances

Studies were conducted to evaluate the impact of potential endogenous and exogenous interfering substances on the performance of the T2Bacteria Panel. These substances were added to negative whole blood samples or to whole blood samples multi-spiked with either *E. coli*, *P. aeruginosa*, and *E. faecium*, or *K. pneumoniae* and *S. aureus* at 2-3x LoD. Three replicate samples were run for each interfering substance tested.

Tables 6a and 6b summarize the endogenous and exogenous substances and the maximum concentrations at which they were tested. All of the substances were tested in excess of standard reference or physiological levels and did not interfere with the performance of the assay with the exception of Ferumoxytol (Feraheme). Initially, Ferumoxytol was tested at 618 µg/mL, which is three fold higher than its t_{max} of 206 µg/mL, but was found to be inhibitory to the performance of the T2Bacteria Panel. Dilutions of Ferumoxytol were performed and it was determined that concentrations ≥ 21 µg/mL interfere with the performance of the T2Bacteria Panel.

Table 6a: Endogenous Substances Tested, No Interference Observed	
Substance	**Concentration**
Albumin	60 g/L
ALT	120 U/liter
AST	144 U/liter
Bilirubin (conjugated)	342 µmol/L
Bilirubin (unconjugated)	342 µmol/L
Creatinine	50 mg/L
Gamma Globulin	60 g/L
Hemoglobin	22.8 – 23.9 g/dL*
Human DNA	2.2 µg/mL
Lactoferrin	7.5 µmol/L
Urea	42.9 mmol/L
White Blood Cells (buffy coat)	2.08×10^7 -2.48×10^7 WBC/mL*
Lipemia (intralipid to mimic triglycerides)	3270 mg/dL

*For hemoglobin and white blood cells, the concentration tested varied between sample types.

Table 6b: Exogenous Substances Tested, No Interference Observed			
Substance	**Concentration**	**Substance**	**Concentration**
Azithromycin (Zithromax)	15.3 µmol/L	Fluconazole	245 µmol/L
Amphotericin B Trihydrate	240 µg/mL	Gentamicin sulfate	21 µmol/L
Ampicillin	152 µmol/L	Heparin	3,000 U/L
Caspofungin	52.8 µg/mL	Isovue 370	180 µL per 4 mL vacutainer
Cefazolin Sodium Salt	2.643 mmol/L	Linezolid	55.8 µg/mL
Cefepime Hydrochloride	492 µg/mL	Lisinopril	0.74 µmol/L
Cefoxitin Sodium Salt	180 µg/mL	Magnevist (gadopentetate dimeglumine)	1.5 mM
Ceftazidime Pentahydrate	487 µg/mL	Meropenem trihydrate	186 µg/mL
Ciprofloxacin	30.2 µmol/L	Metronidazole	701 µmol/L
Clindamycin HCl	89.1 µmol/L	Micafungin	90 mg/L
Cytarabine	32.4 µg/mL	Piperacillin/Pipril	117 µg/mL
Dexamethasone	1.53 µg/mL	Primaxin, 50:50 ratio of Imipenem: Cilastatin	528 µg/mL
EDTA	5.4 mg/mL	Tazobactam (Tazobac)	18.9 µg/mL
		Vancomycin	103 µg/mL

vii. Summary of False Positive Results

The false positive rates observed during analytical testing for each channel of the T2Bacteria Panel are shown in Table 7**.** Overall, false positive rates observed during verification testing were similar across all studies.

Table 7: Summary of False Positive Results in Analytical Studies					
Study	**Efm**	**Eci**	**Kp**	**Pa**	**Sa**
LoD	0.0%	2.0%	0.1%	0.2%	0.0%
5x LoD	0.0%	0.0%	0.0%	0.0%	0.0%
Single vs. Multi	0.0%	1.6%	0.0%	0.0%	0.0%
Interfering Substances	0.2%	2.8%	0.9%	4.3%	0.4%
Analytical Reactivity	0.0%	3.0%	0.0%	0.4%	0.0%
Competitive Inhibition	0.4%	3.2%	0.0%	1.7%	0.2%
Analytical Specificity	0.0%	2.9%	0.0%	0.3%	0.0%
Reproducibility	0.0%	3.7%	0.0%	0.6%	0.0%
Total	**0.1%**	**2.6%**	**0.2%**	**1.5%**	**0.1%**

viii. Summary of Invalid and Indeterminate Results

The invalid and indeterminate rates observed for all samples tested in the verification studies were recorded (Table 8). Excluding interfering substances, invalid rates remained low across all of the studies at an average rate of 0.3%. Interfering substances had an exceptionally high invalid rate of 4.9% due to the nature of the study being the evaluation of substances that interfere with the T2Bacteria Panel. The indeterminate rate for the *E. coli* channel ranged from 0% to 1.3% across the verification studies, and in total was 0.9% in verification considering all studies or 0.8% after excluding the interfering subtances study.

Table 8: Summary of Invalid and Indeterminate Rate Observed in Analytical Studies		
Study	**Invalid Rate**	**Indeterminate rate (*E. coli* channel only)**
LoD	0.5%	1.3%
LoD subset - *E. coli* spikes at 11 CFU/mL	0.0%	0.8%
5x LoD	0.0%	0.0%
Single vs multi	0.0%	0.0%
Interfering Substances	4.9%	1.1%
Analytical Reactivity	0.0%	0.0%
Analytical Specificity	0.2%	0.7%
Reproducibility	0.0%	0.0%
Total	**1.7%**	**0.9%**
Total without Interfering Substances	**0.3%**	**0.8%**

Clinical Performance Evaluation

The performance of 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 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 was tested prospectively.

Due to the low prevalence of the organisms contained in the Panel, an additional 250 contrived specimens were evaluated at three sites. Contrived specimens were prepared by spiking bacteria at defined concentrations (CFU/mL) into healthy donor whole blood. A total of 50 strains of each of the five bacterial species (250 strains total) were used to prepare the contrived specimens. Further, an additional 100 blood samples not spiked with T2Bacteria Panel members were also evaluated as part of the contrived arm of the study.

Table 9 summarizes the overall PPA (sensitivity) and NPA (specificity) from the prospective and contrived arms of the study. The PPA (sensitivity) ranged from 81.3% to 100% and the NPA (specificity) ranged from 95.5% to 100%. Details of the individual arms of the study are summarized in the respective sections below.

Table 9. Sensitivity (PPA) and and Specificity (NPA) from Combined Prospective and Contrived Arms of the T2Bacteria Clinical Study					
Target Species	**Clinical Study Arm**	**PPA[1]**		**NPA[2]**	
		PPA	**95% CI**	**NPA**	**95% CI**
E. faecium	Contrived	100% (40/40)	91.2 - 100%	100% (300/300)	98.7 - 100%
	Prospective	100% (1/1)	20.7 - 100%	99.4% (1417/1426)	98.8 - 99.7%
S. aureus	Contrived	92.3% (36/39)	79.7 - 97.3%	100% (300/300)	98.7 - 100%
	Prospective	81.3% (13/16)[3]	57.0 - 93.4%	98.0% (1383/1411)	97.1 - 98.6%
K. pneumoniae	Contrived	100% (40/40)	91.2 - 100%	99.3% (298/300)	97.6 - 99.8%
	Prospective	100% (6/6)	61.0 - 100%	98.5% (1399/1421)	97.7 - 99.0%
P. aeruginosa	Contrived	97.4% (38/39)	86.8 - 99.5%	97.7% (293/300)	95.3 - 98.9%
	Prospective	100% (5/5)	56.6 - 100%	97.7% (1389/1422)	96.8 - 98.3%
E. coli	Contrived	90.9% (20/22)	72.2 - 97.5%	97.3% (292/300)	94.8 - 98.6%
	Prospective	90.9% (10/11)[4]	62.3 - 98.4%	95.0% (1345/1416)[5]	93.7 – 96.0%

[1]Positive Percent Agreement (PPA) or Sensitivity was calculated against samples with titer levels at or above limit of detection (LoD) in Contrived Arm and blood culture positives in Prospective Arm.
[2]Negative Percent Agreement (NPA) or Specificity was 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.
[3]One subject was blood culture positive for *S. aureus* but negative in the first blood sample and *S. aureus* positive in the second concurrently collected blood sample tested by T2Bacteria Panel. Data shown reflects first result, not second result.
[4]One subject was blood culture positive for *E. coli* but negative in the first blood sample and *E. coli* positive in the second concurrently collected blood sample tested by T2Bacteria Panel. Data shown reflects first result, not second result.
[5]Of the total 1416 blood culture negative subjects, 8 (0.6%) yielded indeterminate results for the *E. coli* channel.

Prospective Arm: T2Bacteria Panel Performance vs. Blood Culture

In the prospective arm of the study, the overall positivity rate for bacterial blood culture was 6.2%, with 2.7% specific for target organisms contained in the T2Bacteria Panel, whereas the overall positivity rate for the T2Bacteria Panel was 13.3%. The PPA (sensitivity) of the T2Bacteria Panel against blood culture ranged from 81.3% to 100% depending upon bacterial species. The NPA (specificity) of the T2Bacteria Panel against blood culture ranged from 95.5% to 99.4%, where all channels showed an NPA of > 97.5% with exception of *E. coli* at 95.5% (Figure 1; Table 10).

Figure 1: T2Bacteria Panel Performance as Compared to Blood Culture

Eci

		Blood culture +	Blood culture -	
T2	+	10	63	73
	Ind	0	8	8
	-	1	1345	1346
		11	1416	1427

	Value	- 95% CI	+ 95% CI
PPA	90.9%	62.3%	98.4%
NPA	95.0%	93.7%	96.0%

Efm

		Blood culture +	Blood culture -	
T2	+	1	9	10
	-	0	1417	1417
		1	1426	1427

	Value	- 95% CI	+ 95% CI
PPA	100.0%	20.7%	100.0%
NPA	99.4%	98.8%	99.7%

Kp

		Blood culture +	Blood culture -	
T2	+	6	22	28
	-	0	1399	1399
		6	1421	1427

	Value	- 95% CI	+ 95% CI
PPA	100.0%	61.0%	100.0%
NPA	98.5%	97.7%	99.0%

Pa

		Blood culture +	Blood culture -	
T2	+	5	33	38
	-	0	1389	1389
		5	1422	1427

	Value	- 95% CI	+ 95% CI
PPA	100.0%	56.6%	100.0%
NPA	97.7%	96.8%	98.3%

Sa

		Blood culture +	Blood culture -	
T2	+	13	28	41
	-	3	1383	1386
		16	1411	1427

	Value	- 95% CI	+ 95% CI
PPA	81.3%	57.0%	93.4%
NPA	98.0%	97.1%	98.6%

Table 10: T2Bacteria Panel Performance as Compared to Blood Culture

Species	PPA (Sensitivity)		NPA (Specificity)	
	PPA	95% CI	NPA	95% CI
E. coli	90.9% (10/11)	62.3 - 98.4%	95.0% (1345/1416)[1]	93.7 – 96.0%
E. faecium	100% (1/1)	20.7 - 100%	99.4% (1417/1426)	98.8 - 99.7%
K. pneumoniae	100% (6/6)	61.0 - 100%	98.5% (1399/1421)	97.7 - 99.0%
P. aeruginosa	100% (5/5)	56.6 - 100%	97.7% (1389/1422)	96.8 - 98.3%
S. aureus	81.3% (13/16)	57.0 - 93.4%	98.0% (1383/1411)	97.1 - 98.6%

[1]Of the total 1416 blood culture negative subjects, 8 (0.6%) yielded indeterminate results for the *E. coli* channel.

Both freshly collected and frozen blood samples were tested with the T2Bacteria Panel in the Prospective arm. Of the 1,427 patient specimens tested, 672 were fresh and 755 were frozen. An analysis was performed and demonstrated that the fresh and frozen samples did not show a statistically significant difference in PPA or NPA ($p > 0.12$; Table 11).

Table 11: T2Bacteria Panel Performance on Fresh v Frozen Blood

		PPA (Sensitivity)		NPA (Specificity)	
Species	Sample Type	Value	TP / (TP + FN)	Value	TN / (TN + FP)
Eci	Fresh	100.0%	4 / 4	94.6%	630 / 666
	Frozen	85.7%	6 / 7	96.4%	715 / 742
Efm	Fresh	100.0%	1 / 1	99.3%	666 / 671
	Frozen	---	0 / 0	99.5%	751 / 755
Kp	Fresh	100.0%	4 / 4	98.2%	656 / 668
	Frozen	100.0%	2 / 2	98.7%	743 / 753
Pa	Fresh	100.0%	2 / 2	97.9%	656 / 670
	Frozen	100.0%	3 / 3	97.5%	733 / 752
Sa	Fresh	80.0%	8 / 10	97.7%	647 / 662
	Frozen	83.3%	5 / 6	98.3%	736 / 749

Contrived Arm

Results for the Contrived arm were further analyzed based on the spiked pathogen concentration (either above or below the LoD). The positivity rates for contrived clinical testing were consistent with the results determined for the analytical LoD levels, as shown in Table 12.

Table 12: PPA for Contrived samples above and below the Limit of Detection

Contrived Sample Type	LoD (CFU/mL)	< LoD		≥ LoD	
		Sensitivity (PPA)	95% CI	Sensitivity (PPA)	95% CI
E. coli	11	67.8% (19/28)[1]	49.3 – 82.1%	90.9% (20/22)[2]	72.2 - 97.5%
E. faecium	5	60.0% (6/10)	31.3 - 83.2%	100% (40/40)	91.2 - 100%
K. pneumoniae	2	50.0% (5/10)	23.7 - 76.3%	100% (40/40)	91.2 - 100%
P. aeruginosa	5	63.6% (7/11)	35.4 - 84.8%	97.4% (38/39)	86.8 - 99.5%
S. aureus	2	18.2% (2/11)	5.1 - 47.7%	92.3% (36/39)	79.7 - 97.3%

[1]Of the total 28 samples spiked at < LoD, 2 (7%) yielded indeterminate results for the *E. coli* channel.
[2]For all samples spiked with *E. coli* at >1 CFU/mL, the positivity rate was 36/40 yielding a PPA of 90.0% (77.0 – 96.0% 95% CI).

Evaluation of False Positive Results

Overall, in the prospective study, there were 190 T2 positive results consisting of 35 T2+/BC+ concordant results and 155 T2+/BC- potential false positive results. As shown in Table 13, of the 155 potential false positive results, 39 represented patients with an additional positive blood culture at a different blood draw within ±14 days of the T2 draw and 30 results 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. An additional 23 results were obtained from patients who had other non-blood specimens positive for the same target organism (collected ± 14 days from the positive T2 specimen). Based on this analysis, 63 of the 190 T2 positive results (33%) or 63 of the 155 potential false positive results (41%) were not associated with evidence of infection.

Table 13: Summary of T2(+) / BC(-) Discordant Analysis in Prospective Arm

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
E. faecium	9	2	2	44.4% (4/9)	33.3% (3/9)	22.2% (2/9)
E. coli	63	12	9	33.3% (21/63)	12.7% (8/63)	54.0% (34/63)
K. pneumoniae	22	6	8	63.6% (14/22)	13.6% (3/22)	22.7% (5/22)
P. aeruginosa	33	3	8	33.3% (11/33)	12.1% (4/33)	54.5% (18/33)
S. aureus	28	16	3	67.9% (19/28)	17.9% (5/28)	14.3% (4/28)
Total	**155**	**39**	**30**	**44.5% (69/155)**	**14.8% (23/155)**	**40.7% (63/155)**

[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 2).

[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.

[4] Other cultures from non-blood sample matrices positive for the T2 species identified within ± 14 days of collection of the T2 sample.

Further investigation identified reagents contamination as the likely source for the false positive results from patients with no evidence of infection. T2 Biosystems implemented improved reagent testing methods and release criteria with the overall goal of reducing the rate of false positive results that can be attributed to reagents contamination. As shown in Table 14, after these improvements reagents contamination was observed at levels of ≤1% for all targets.

Table 14: Positivity of T2Bacteria Panel in QCheck NEG samples before and after improvements					
Species	**Efm**	**Eci**	**Kp**	**Pa**	**Sa**
Before Improvements	0.00% (0/875)	1.94% (17/875)	0.23% (2/875)	0.91% (8/875)	0.00% (0/875)
After Improvements	0.00% (0/286)	1.05% (3/286)	0.00% (0/286)	0.35% (1/286)	0.00% (0/286)

Archived samples were tested for 43 of the 52 discordant T2(+) / BC(-) samples that were originally positive for *E. coli* (30 samples tested) or *P. aeruginosa* (13 samples tested) but not associated with any other evidence of infection. Upon retesting after improvements, none of the archived samples were positive for *E. coli*, suggesting that the original 30 tested *E. coli* positive samples were most likely false positive results. Two of the archived samples were positive for *P. aeruginosa* from patients who were originally T2 positive for *P. aeruginosa*, suggesting that these 2 samples were most likely true positive results and the remaining 11 tested samples were most likely false positive results for *P. aeruginosa*.

After improvements, additional testing was completed on 286 QCheck negative controls and 120 K_2EDTA blood samples obtained from healthy donors. False positives were observed only for *E. coli* (1.7%) and *P. aeruginosa* (1.7%) in the blood samples and only for *E. coli* (1.0%) and *P. aeruginosa* (0.3%) in the QCheck negative controls.

Prospective and Contrived arm, Invalid and Indeterminate rate

The Prospective arm showed an overall invalid rate of 0.5% and an indeterminate rate of 0.6%, where the indeterminate result applies to the *E. coli* channel only. Similarly, the Contrived arm showed a 0.0% invalid rate and 0.6% indeterminate rate. In aggregate, the combined Prospective and Contrived arms generated a total invalid rate of 0.4% and total indeterminate rate of 0.6%.