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

I Background Information:

A 510(k) Number

K251495

B Applicant

Bruker Daltonics GmbH & Co. KG

C Proprietary and Established Names

MBT Compass HT CA Software; MBT FAST Shuttle US IVD

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QBN, QNJ	Class II	21 CFR 866.3378 - Clinical Mass Spectrometry Microorganism Identification And Differentiation System	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain 510k clearance for:

1. MBT Compass HT CA Software for use with the MBT CA System and MBT Sepsityper
2. MBT Fast Shuttle US IVD accessory for use with the MBT CA System and MBT Sepsityper

B Measurand:

See Indications for Use

C Type of Test:

The MBT CA System is a qualitative *in vitro* diagnostic device intended for the identification and differentiation of microorganisms cultured from human specimens using matrix-assisted laser desorption/ionization - time of flight (MALDI-TOF) mass spectrometry.

The MBT Sepsityper system is an *in vitro*, qualitative device for species identification of Gram positive and negative bacteria and yeasts in positive blood cultures using MALDI-TOF mass spectrometry.

III Intended Use/Indications for Use:

A Intended Use(s):

The MALDI Biotyper CA System is a mass spectrometer system using matrix-assisted laser desorption/ionization - time of flight (MALDI-TOF) for the identification and differentiation of microorganisms cultured from human specimens.

The MALDI Biotyper CA System is a qualitative in vitro diagnostic device indicated for use in conjunction with other clinical and laboratory findings to aid in the diagnosis of bacterial and yeast infections.

B Indication(s) for Use:

The MBT Sepsityper is a qualitative in vitro diagnostic device consisting of an MBT-CA (Sepsityper) software extension and a reagent kit (MBT Sepsityper Kit US IVD) for use in conjunction with other clinical and laboratory findings to aid in the early diagnosis of bacterial and yeast infections from positively flagged blood cultures using the MALDI Biotyper CA System.

The MBT Sepsityper Kit US IVD is a disposable blood culture processing device that includes associated reagents that are intended to concentrate and purify microbial cells from blood culture samples identified as positive by a continuous monitoring blood culture system and confirmed to demonstrate the presence of a single organism as determined by Gram stain. This sample preparation manual method is performed by laboratory health professionals in a clinical diagnostic setting. Subculturing of positive blood cultures is necessary to recover organisms for identification of organisms not identified by the MBT-CA System, for susceptibility testing and for differentiation of mixed growth. Positive MBT Sepsityper results do not rule out co-infection with organisms that may not be detected by the MBT-CA System.

Results of the MBT Sepsityper should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Results of the MBT Sepsityper should be correlated with Gram stain results and used in conjunction with other clinical and laboratory findings to aid in the diagnosis of bacterial and yeast bloodstream infections.

Organisms recovered from positive blood culture bottles that are suitable for identification using the MBT Sepsityper Kit US IVD and MBT-CA Systems are listed in the MALDI Biotyper CA System Package Insert Reference Library.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

MBT-CA System including:

- MALDI Biotyper CA System
- MALDI Biotyper smart CA System
- MALDI Biotyper sirius CA System

Optional Instruments

- MBT Galaxy System - US IVD
- MBT Pilot System - US IVD
- MBT Sepsityper US IVD

IV Device/System Characteristics:

A Device Description:

The MALDI Biotyper CA System uses MALDI-TOF mass spectrometry technology for the identification of organisms isolated from clinical samples. Identification can be performed from an isolated colony or from positive blood cultures. With the use of the Sepsityper US IVD kit, blood culture samples identified as positive by a continuous monitoring blood culture system and confirmed to demonstrate the presence of a single organism morphology as determined by Gram Stain, may be concentrated and purified to be analyzed by the system. The sample material is transferred to a target plate, dried, and overlaid with a matrix.

The MALDI process transforms the proteins and peptides from the isolated microorganisms into positively charged ions. This is achieved by irradiating the matrix-sample composite with a UV laser. The matrix absorbs laser energy and transfers protons to the intact proteins or peptides in the gas phase. These ions are electrostatically accelerated and arrive in the flight tube at a mass-dependent speed. Because different proteins/peptides have different masses, ions arrive at the detector at different times (time of flight). The MBT-CA System measures the time (in the nanosecond range) between pulsed acceleration and the corresponding detector signal of the ions, and the time is converted into an exact molecular mass.

The highly abundant microbial proteins (chiefly ribosomal) result in a mass spectrum with a characteristic mass and intensity distribution pattern. This pattern is species-specific for many bacteria and yeasts and can be used as a "molecular fingerprint" to identify a test organism. The spectrum of the unknown test organism, acquired through the MBT Compass HT CA software of the MBT-CA System, is electronically transformed into a peak list. Using a biostatistical algorithm, this peak list is compared to reference peak lists of organisms in the MBT-CA Reference Library and a score between 0.00 and 3.00 is calculated. The higher the score, the higher the degree of similarity to a given organism in the MBT-CA Reference Library. The score ranges reflect the probability of organism identification.

MBT FAST Shuttle US IVD

The MBT FAST Shuttle US IVD is an optional hardware accessory that may be used for drying the samples deposited on the MALDI target plate under controlled conditions, as shown in Figure 1:

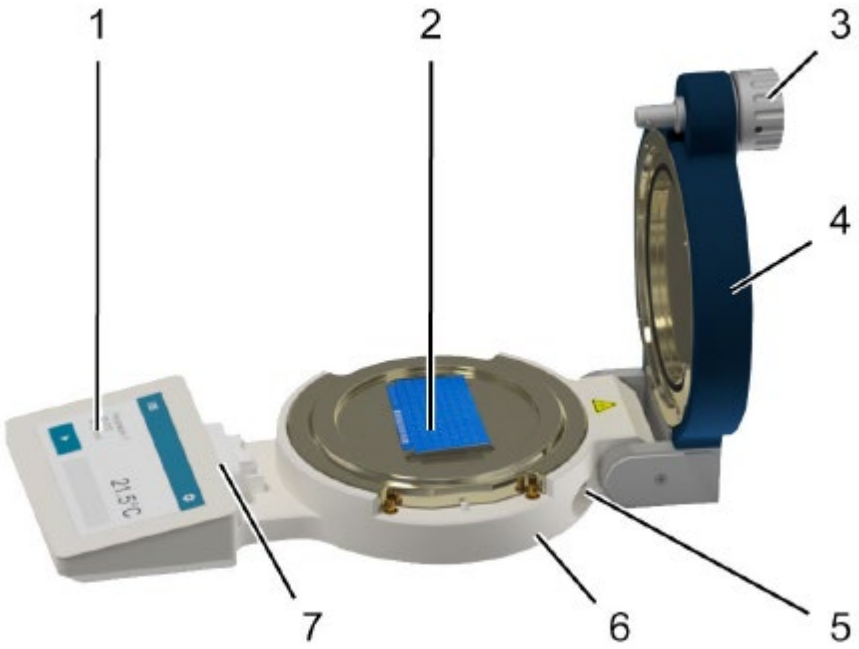

Figure 1 : MBT FAST Shuttle US IVD: **1.** Touch display**, 2.** MBT MSP Biotarget Adapter, **3**. Rotary lid lock with sensor, **4.** Heated lid, **5**. Socket for power supply, **6**. Heated base, **7.** Standby LED

MBT Compass CA Software

The MBT Compass HT CA software is the successor version of MBT-CA System software in the MBT-CA System. In addition, the optional MBT HT Sepsityper CA Module required only for identification of samples from positive blood culture samples/cultures is available.
To allow for easier handling, this software has the ability to also inform user about hardware status. Similarly, to allow users better information on the provided outcome, the MBT Compass HT CA software:

- Provides the second-best match, along with consistency categorization.
- Provides matching hints (i.e., additional information useful in interpreting results).
- Allows users to inspect details about executed Bacterial Test Standard BTS QC procedures (especially helpful in case the BTS-QC did fail).
- Allows users to inspect spectra.
- Allows for repeated LIMS export and to report sample subsets.

B Principle of Operation:

1. **MBT Fast Shuttle**

   The user operates the MBT Fast Shuttle IVD as follows:

   1. User opens the lid, selects the sample drying workflow from the menu and switches on the workflow.

2. The base is heated to 35°C from room temperature for 30 minutes.
3. The user then inserts the MALDI target on the heated base of the MBT FAST Shuttle and leaves the lid open.
4. The user then performs sample preparation and drying steps on the instrument as follows:

    a) Smears bacterial samples on to the target.
    b) Pipets matrix (HCCA)/FA according to the desired sample preparation method.
    c) Let the droplets dry completely.
    d) Switches the heater off if applicable (the sample drying workflow is automatically stopped after 30 minutes).
    e) Removes the MALDI target for insertion into the instrument for analysis.

2. **MBT Compass CA Software**

    The user begins by logging into the Compass CA system software. The instrument run is defined based on a list of sample identifiers assigned to appropriate target plate positions. The same MALDI target plate can support different sample types, by selecting the appropriate sample type in the software, with no further user intervention the sample is measured and processed. Each run starts with an automatic mass calibration of the instrument followed by the measurement of bacterial test standard (BTS) preparation. The run continues only if the acquired BTS spectra fulfills predefined quality criteria (BTS-QC passed). In this case all samples defined in the MBT run are measured and identified (matched against the reference patterns provided in the database). A successfully completed MBT run finally assigns an identification result to each sample.

C Instrument Description Information:

1. Instrument Name:

    MBT-CA System including:
    - MALDI Biotyper CA System
    - MALDI Biotyper smart CA System
    - MALDI Biotyper sirius CA System

    Optional Instruments
    - MBT Galaxy System - US IVD
    - MBT Pilot System - US IVD
    - MBT Sepsityper US IVD
    - MBT Fast Pilot US IVD

2. Specimen Identification:

    Specimen Identification is identical to K193419.

3. Specimen Sampling and Handling:

    Specimen Sampling and handling is identical to K193419, with the addition of the optional MBT Fast Pilot US IVD for automated sample drying.

4. Calibration:

Calibration is achieved using the US IVD Bacterial Test Standard (BTS), an in vitro diagnostic product used for quality control and validation. US IVD BTS contains a manufactured extract of *Escherichia coli* DH5 alpha that demonstrates a characteristic peptide and protein profile mass spectrum, when tested on the MALDI Biotyper CA System. This reagent is spiked with two additional proteins that extend the upper boundary of the mass range of the US IVD BTS. The overall mass range covered by US IVD BTS is 3.6 to 17 kDa. If US IVD BTS does not meet all required performance specifications, the test run will be invalid.

5. Quality Control:

   The user will follow local, state and/or federal regulations for quality control requirements.

V Substantial Equivalence Information:

A Predicate Device Name(s):

MBT Sepsityper

B Predicate 510(k) Number(s):

K193419

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251495 (Candidate Device)	K193419 (Predicate Device)
Device Trade Name	MBT-CA System with MBT Compass HT CA MBT FAST Shuttle US IVD	MBT Sepsityper/ MALDI Biotyper CA (MBT-CA) System, MALDI Biotyper (MBT-CA) smart CA System, MALDI Biotyper (MBT-CA) sirius CA System
General Device Characteristic Similarities		
Indications For Use	The MBT Sepsityper is a qualitative in vitro diagnostic device consisting of a MBT-CA software extension (Sepsityper Software Module US IVD) and a reagent kit (MBT Sepsityper Kit US IVD) for use in conjunction with other clinical and laboratory findings to aid in the early diagnosis of bacterial and yeast infections from positively flagged blood cultures using the MALDI Biotyper CA System. The MBT Sepsityper Kit US IVD is a disposable blood culture processing device that includes associated reagents that are intended to concentrate and purify microbial cells from blood culture samples identified as positive by a continuous monitoring blood culture system and confirmed to demonstrate the presence of a single organism as determined by Gram stain.	Same

	This sample preparation manual method is performed by laboratory health professionals in a clinical diagnostic setting. Subculturing of positive blood cultures is necessary to recover organisms for identification of organisms not identified by the MBT-CA System, for susceptibility testing and for differentiation of mixed growth. Positive MBT Sepsityper results do not rule out co-infection with organisms that may not be detected by the MBT-CA System. Results of the MBT Sepsityper should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Results of the MBT Sepsityper should be correlated with Gram stain results and used in conjunction with other clinical and laboratory findings to aid in the diagnosis of bacterial and yeast bloodstream infections.	
Sample Type	Isolated colonies, positive blood cultures	Same
Sample Measurement Principle	MALDI-TOF mass spectrometry	Same
Analyzed Mass Range	3,000 – 15,000 m/z (Isolated Colonies) 4,000 – 15,000 m/z (Sepsityper samples)	Same
Search Algorithm	Finds the most similar reference pattern by matching all patterns from the reference pattern library against the peak list of the measured spectrum (of the unknown sample).	Same
Search Score Range	Single colony from agar plate: • High Confidence ID: 2.00 - 3.00; • Low Confidence ID: 1.70 - 1.99; • No Organism ID Possible: 0.0 - 1.69 MBT Sepsityper Samples: • High Confidence ID: 1.80 - 3.00; • Low Confidence ID: 1.60 - 1.79; • No Organism ID Possible: 0.00 - 1.59	Same
Output Design - Mixed culture hints	Single colonies: No Sepsityper samples: Yes	Same
General Device Characteristic Differences		
Sample preparation.	Matrix solution (US IVD HCCA) is added to the inoculated target spot and dried. Solution can be deposited manually or with MBT Galaxy System. Drying can be performed at room temperature or with use of MBT FAST Shuttle US IVD.	Matrix solution (US IVD HCCA) is added to the inoculated target spot and dried. Solution can be deposited manually or with MBT Galaxy System. Drying can be performed at room temperature.
Calculation Time	MBT Compass HT CA can use all processor cores for a parallel calculation of results.	MBT-CA System Software uses one processor core.

Software access control	In MBT Compass HT CA user management for controlling accessibility of software features based on dedicated user roles are offered and additional features for supporting 21 CFR Part 11 compliance are implemented.	In MBT-CA System SW, no authentication is required when starting the software and no support is provided for the 21 CFR Part 11 regulations.
Spectra Visualization	Users may visualize recorded spectra in MBT Compass HT CA software	User cannot visualize spectrum in MBT CA software
Display of matches	MBT Compass HT CA software displays 2nd best match along with a consistency category ranking based on the based on the confidence level of the best and second-best matches.	MBT CA Software displays best match only
Final Output	MBT Compass HT CA allows for declaring a low confidence result as final (no further preparation method needed).	MBT-CA Software requires going to the next preparation method (eDT, EXT) to enhance low confidence results.
Tuning and Maintenance	The MBT Compass HT CA software has implemented IDealTune. The IDealTune algorithm utilizes measurement of the BTS-QC sample to keep a well-tuned MBT CA System in an optimal state.	The MBT-CA System requires regular maintenance. Tuning can be performed remotely by Bruker support through Tune-Ups.

VI Standards/Guidance Documents Referenced:

Document	Title	Publisher	Applicable Study
Special Controls under 21 CFR 866.3378	Special Controls for Clinical mass spectrometry microorganism identification and differentiation system	FDA/CDRH	All Studies
IEC/EN 61326-1Ed.3.0 b:2020	Electrical equipment for measurement, control, and laboratory use - EMC requirements - Part 1: General requirements	IEC/EN	EMC
FDA Software Guidance	Content of Premarket Submissions for Device Software Functions Guidance for Industry and Food and Drug Administration Staff 2023	FDA	Software
FDA Cybersecurity Guidance	Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions: 2025	FDA	Cybersecurity

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

a. Precision

This study was performed at the manufacturer's internal site to assess the repeatability of identification of microorganisms using the MBT CA System with the option of MBT FAST Shuttle for the drying procedure. A panel of ten microorganisms consisting of aerobic and anaerobic Gram-negative and Gram-positive bacteria, and yeast organisms were tested by the three sample preparation methods (DT, eDT and Ext) of MBT and Sepsityper workflows.

Microbial samples and BTS (quality control) were applied to targets and dried at 35 (± 1) °C using the MBT FAST Shuttle. In the next step MALDI matrix was applied and again dried at 35 (± 1) °C using the MBT FAST Shuttle. Samples were measured with the MBT System and obtained mass spectra were analyzed using MBT Compass software and library.

One operator performed all method procedures for 2 separate runs for both the MBT and Sepsityper workflows. In total, 120 mass spectra were obtained. The number of correct identification results was used to determine the percentage of correct results for each method and workflow. The matched percentages of correct results obtained by one operator across two runs at the manufacturer's internal site were used to calculate repeatability. These results are summarized in Table 1 and demonstrate acceptable repeatability for both workflows.

Table 1. Precision/Repeatability Study Results

Method	MBT workflow		Sepsityper workflow	
	Run 1	Run 2	Run 1	Run 2
DT	100%	90%	100%	100%
eDT	90%	100%	100%	100%
Ext	100%	100%	100%	100%
Average	96.67%	96.67%	100%	100%
Overall average	**96.67%**		**100%**	

b. Reproducibility

This study was performed at three clinical sites to assess reproducibility of identification of microorganisms using the MBT CA System with the MBT FAST Shuttle US IVD. All study sites used the same set of 10 microorganisms as the precision/repeatability study, to allow for direct comparison of results.

For the MBT workflow at each site, 3 replicates of the 10 microorganisms were ran for the three sample preparation methods with 2 runs/day for 5 days for a total of 900 samples. For the Sepsityper workflow an abbreviated panel of 5 microorganisms was run with the same

study protocol for a total of 450 samples per study site. The overall results are shown in Table 2.

Table 2. Reproducibility Study Results

Type of workflow	Number of samples per study site	% Successful ID rate (High+Low Confidence ID)[a]			
		Site 1	Site 2	Site 3	Total
MBT workflow (DT+eDT+Ext)	900	885/900 (98.3%)	856/900 (95.1%)	876/900 (97.3%)	2617/2700 (96.9%)
Sepsityper workflow (DT+eDT+Ext)	450	445/450 (98.8%)	384/450 (85.3%)	375/450 (83.3%)	1204/1350 (89.1%)

[a] No incorrect identifications were observed in this study.

2. Linearity:

   Not applicable; qualitative assay

3. Analytical Specificity/Interference:

   As the analytical principle of the device is unchanged, this data is leveraged from K194319, DEN170081, and K130831.

4. Assay Reportable Range:

   The assay reportable ranges are unchanged from K193419 and K130831 and are summarized in Table 3:

Table 3. Summary of Reportable Ranges for BIotyper and Sepsityper

Workflow	Instrument Mass Range	ID Score Ranges
MALDI Biotyper	3,000-15,000 m/z	• High Confidence ID: 2.00- 3.00; • Low Confidence ID: 1.70-1.99; • No Organism ID Possible: 0.0 - 1.69
MBT Sepsityper	4,000-15,000 m/z	• High Confidence ID: 1.80-3.00; • Low Confidence ID: 1.60-1.79; • No Organism ID Possible: 0.00-1.59

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

As the analytical principle of the device is unchanged, this data is leveraged from K194319, DEN170081, and K130831

6. Detection Limit:

   As the analytical principle of the device is unchanged, this data is leveraged from K194319, DEN170081, and K130831

7. Assay Cut-Off:

   As the analytical principle of the device is unchanged, this data is leveraged from K194319, DEN170081, and K130831

8. Carry-Over:

   As the analytical principle of the device is unchanged, this data is leveraged from K194319, DEN170081 and K130831.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   a. ***Sample Drying Comparison; Fast Shuttle vs. Predicate***

   This comprehensive study was performed at two clinical sites and the manufacturer's site to assess the performance of the MBT FAST Shuttle – US IVD sample drying device in comparison to the sample drying at room temperature.

   Ten (10) microorganisms covering aerobic and anaerobic Gram-negative and Gram-positive bacteria as well as yeast were shipped to each external study site. One operator at each study site performed the DT, eDT, and Ext procedure with each of the ten (10) strains and a blood culture sample using both drying methods. In total, these thirty-one (31) samples were spotted in triplicates resulting in ninety-three (93) mass spectra. This number of mass spectra was collected at all three (3) study sites. In total, 279 mass spectra of air-dried (RT, 20 – 25 °C) and 279 mass spectra of MBT FAST Shuttle dried samples were generated. The log (score) values obtained for each spectrum from all study sites and preparation methods were used to calculate results shown in Tables 4 and 5, which illustrate the equivalent performance of the two sample preparation methods.

Table 4. Comparison Study Results by Preparation Type

Sample preparation method	Number of spots	Log(score)		
		Log(score) mean ± SD Air-dried samples	Mean Log (score) ± SD MBT FAST Shuttle dried samples	Difference
DT	90	2.30 ± 0.21	2.27 ± 0.32	0.03

eDT	90	2.26 ± 0.33	2.32 ± 0.32	-0.06
Ext	90	2.43 ± 0.14	2.43 ± 0.14	0
Sepsityper	9	2.17 ± 0.21	2.27 ± 0.15	-0.1

Table 5. Comparison Study Results by Study Site

Study site	Number of spots	Log(score)		
		Mean Log(score) ± SD Air-dried samples	Mean Log (score) ± SD MBT FAST Shuttle dried samples	Difference
1	93	2.24 ± 0.33	2.26 ± 0.31	-0.02
2	93	2.34 ± 0.19	2.34 ± 0.31	0
3	93	2.40 ± 0.19	2.42 ± 0.16	-0.02
Total (all sites)	279	2.32 ± 0.25	2.34 ± 0.28	-0.02

b. ***Sample Drying Time Comparison: Fast Shuttle vs. Predicate Method:***

This testing was performed at one study site and its goal was to assess drying time of prepared samples using the MBT FAST Shuttle, in comparison to the time needed to dry samples under routine conditions.

A set of ten (10) different microorganisms was prepared by the DT, eDT, and Ext methods and BTS was also prepared on MBT Biotarget 96. All spots were dried either under routine conditions (RT) or applying the MBT FAST Shuttle drying process at elevated temperatures [35 ± (1) °C]. Drying times were measured and compared for both drying procedures. Three (3) independent test series of drying times were performed. Table 6 presents a summary of drying times for all methods. The MBT FAST Shuttle drying process was significantly faster than the sample drying process under routine conditions (air drying time).

Table 6. Sample Drying Time Study Results

Test set	Sample preparation Method	Air drying Time (minutes)	MBT FAST Shuttle Time (minutes)
1	DT	12.95	6.45
	eDT	24.88	12.46
	Ext	21.02	11.25
	IVD BTS	22.12	8.34
2 (Avg. of 2 datasets)	DT	7.8	2.47
	eDT	21.58	7.65
	Ext	12.8	4.80
Mean time (minutes) all methods		**17.59**	**7.63**
95% confidence interval (minutes)		**13.38-21.81**	**3.41- 11.85**

2. Matrix Comparison:

As the analytical principle of the device is unchanged, this data is leveraged from K194319, DEN170081, and K130831.

C Clinical Studies:

1. Clinical Sensitivity and Specificity:

   As the analytical principle of the device is unchanged, this performance data is leveraged from K194319, DEN170081, and K130831.

D Clinical Cut-Off:

See VI.A.4, above.

E Expected Values/Reference Range:

See VI.A.4 above.

F Other Supportive Instrument Performance Characteristics Data:

1. Validation of the IDealTune Function in MBT Compass CA Software

   The performance of the IDealTune (the Auto-Tuning) feature of MBT Compass HT CA software was validated at two laboratory sites, from systems with the software installed under normal operating conditions. From each site, information about the pass rate of the BTS quality check (BTS-QC) was collected over a period of 14-17 months. Based on these results, IDealTune functionality was successfully validated in the devices intended use environment.

2. Acceptance of Low Confidence results

   A retrospective analysis was performed using data previously obtained and used for clearance of the previous versions of the MBT-CA System (K130831, K142677, K 163536, K193419). The purpose of this study was to determine if low confidence results (yellow scores) could be generally accepted as the final result and to confirm that these scores generated by DT and/or eDT preparation methods show no significant differences of species identification compared to the Ext preparation method.

   In total, 15,270 spectra were measured and identified in these clinical studies out of which 1,670 yellow log (scores) were re-analyzed and evaluated in terms of their correctness. Out of the 1,670 DT/eDT samples with low-confidence log (scores), 1,269 samples showed high-confidence species identification results after applying Ext. However, only 7 samples out of the 1,269 samples (0.55%) showed a discordant result after Ext sample preparation was applied compared to DT/eDT. All of the 7 samples with different identifications between DT/eDT and Ext did not express incorrect identifications but could be fully resolved by applying polyphasic taxonomic rules or have been addressed by improvement of the mass spectral reference library.

VIII Proposed Labeling:

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

IX Conclusion:

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

As all blood culture bottles are sub-cultured and growth will be assessed as compared to MBT Sepsityper identification, reduced performance for MBT Sepsityper blood culture identification is acceptable as compared to isolated colony identification. Users should follow the Instructions for Use (IFU) which indicates all results should be reviewed by a trained microbiologist and final organism identification should be based on all relevant information available.