# Rapid Detection Of Bloodstream Infections, Including Molecular Characterization, From Whole Blood

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## Introduction

- Diagnosis of bloodstream infections (BSI) and subsequent treatment with appropriate antimicrobials is dependent upon fast and accurate information about the causative microorganism(s).
- The time taken for blood culture, microbial identification and antimicrobial susceptibility testing (AST), can lead to poor antimicrobial stewardship and patient care.
- Many antimicrobial change decisions are based on the results of a Gram stain, with this being the first result available.
- A rapid test, which can confirm BSI and characterize the causative pathogen(s), would improve antimicrobial stewardship and patient care.

## Method

- SepsiSTAT® is a rapid direct-from-blood molecular test, developed by Momentum Bioscience Ltd, for the detection of BSI, with a time-to-result of < 4 hours.
- Uses whole blood to detect viable microorganisms whilst also providing molecular characterization (Gram status and genus of key infectious organisms).
- Microorganisms are extracted from the sample through capture on magnetic microbeads, followed by Enzymatic Template Generation and Amplification (ETGA®) for ultra-sensitive, universal detection of viable bacterial and fungal species.
- Simultaneously, molecular characterization (Molecular ID) also provides genus/species identification based on total microbial DNA present (from viable cells and cell-free DNA).
- The detection limits of SepsiSTAT® were evaluated for a broad panel of microorganisms, representing 80.4% of BSI reported to Public Health England (2018 report).

## Results

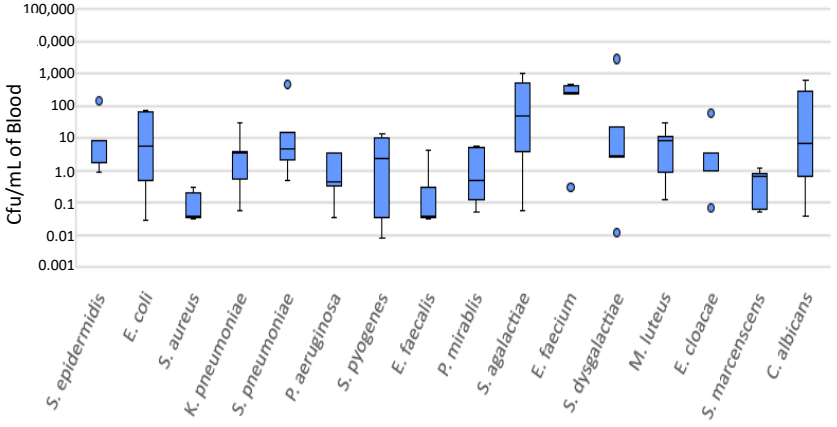


*Figure 1: ETGA results for 16 microorganism panel (n=5). The boxes show the upper/lower quartiles, with the line representing the median cfu/mL. The lines (whiskers) show the lowest and highest detected cfu/mL, with dots representing outliers.*

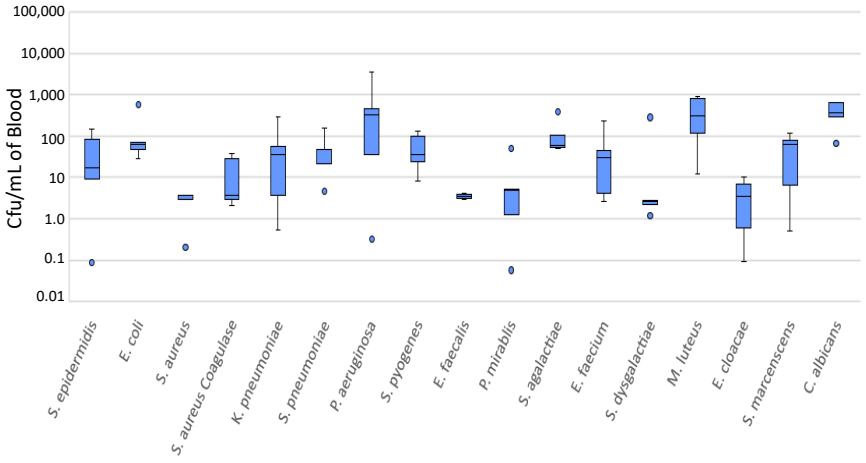


*Figure 2: Molecular ID results for 16 microorganism panel (n=5). The boxes show the upper/lower quartiles, with the line representing the median cfu/mL. The lines (whiskers) show the lowest and highest detected cfu/mL, with dots representing outliers. Note that S. aureus has two SepsID detection channels: Staphylococci and Coagulase*

## Discussion

- This study was carried out with five biological replicates of each of the microorganisms.
- Of the 16 microorganisms tested, all but two had an ETGA median limit of detection (LoD) of < 10 cfu/mL, and of these, five organisms were detected at < 1 cfu/mL. These results demonstrate that 77.4% of monomicrobial infections are detected at < 10 cfu/mL.
- For Molecular ID, 13 of 16 had a median LoD of < 100 cfu/mL, with six organisms being detected at < 10 cfu/mL. This shows that 76.9% of monomicrobial infections are detected at < 100 cfu/mL. Importantly, total microbial DNA in BSI has been shown to have a typical range of 100-10,000 cfu equivalents/mL (Bacconi *et al*).
- For ETGA, of the five ESKAPE organisms tested (*A. baumannii* not tested), four of these are detected at levels < 10 cfu/mL, with only *E. faecium* detected at 260 cfu/mL.
- For Molecular ID, four organisms are also detected at levels < 100 cfu/mL, with only *P. aeruginosa* detected at 336 cfu/mL.

References: Bacconi, Andrea, *et al.* (2014). "Improved sensitivity for molecular detection of bacterial and Candida infections in blood." Journal of clinical microbiology 52.9: 3164-3174.

*Table: Median detections for ETGA and Molecular ID for the 16 microorganisms tested. Key shows cfu/mL blood detection levels and number of microorganisms detected at those levels*

| Organism | PHE Rank | % Infections | Cumulative Infection | ETGA | Molecular ID |
|---|---|---|---|---|---|
| *S. epidermidis* | 1 | 25.7 | 25.7 | 8.4 | 16.8 |
| *E. coli* | 2 | 24.9 | 50.6 | 5.8 | 64.2 |
| *S. aureus (*Coagulase)* | 3 | 7.7 | 58.3 | 0.1 | 3.0/ *3.6 |
| *K. pneumoniae* | 4 | 4 | 62.3 | 3.5 | 34.8 |
| *S. pneumoniae* | 5 | 3.7 | 66 | 4.6 | 47.8 |
| *P. aeruginosa* | 6 | 2.2 | 68.2 | 0.5 | 336.0 |
| *S. pyogenes* | 7 | 2 | 70.2 | 2.4 | 36.0 |
| *E. faecalis* | 8 | 1.8 | 72 | 0.1 | 3.6 |
| *P. mirabilis* | 9 | 1.8 | 73.8 | 0.5 | 5.0 |
| *S. agalactiae* | 10 | 1.6 | 75.4 | 50.8 | 59.0 |
| *E. faecium* | 11 | 1.4 | 76.8 | 260.0 | 30.2 |
| *S. dysgalactiae* | 12 | 1 | 77.8 | 2.9 | 2.7 |
| *M. luteus* | 14 | 0.9 | 78.7 | 8.3 | 312.0 |
| *E. cloacae* | 15 | 0.8 | 79.5 | 1.0 | 3.4 |
| *S. marcescens* | 18 | 0.5 | 80 | 0.6 | 62.6 |
| *C. albicans* | 25 | 0.4 | 80.4 | 6.6 | 368.0 |

**Key:**

| | ETGA | Molecular ID |
|---|---|---|
| <1000 | 16 | 16 |
| <100 | 15 | 13 |
| <10 | 14 | 6 |
| <1 | 5 | 0 |

## Conclusion

- SepsiSTAT® results demonstrate the sensitivity of universal detection of viable microorganisms.
- SepsiSTAT® detects clinically relevant microorganisms at low levels with sensitive and specific detection.
- Current development aims to shorten the time-to-result to < 3 hours.
- Studies in a clinical setting with seek to further demonstrate the efficacy and potential to impact patient care.