Clinical evaluation of the SPECIFIC REVEAL™ Rapid AST System with Gram-negative bacteremia samples in 6 hospitals in France and England

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Background

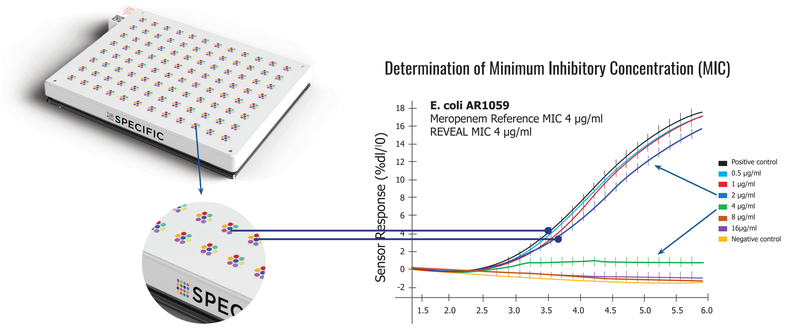
Bloodstream infection is a life-threatening condition requiring immediate initiation of effective antimicrobial therapy. The emergence of resistant (R) Gram-negative (GN) bacteria can compromise the efficacy of empiric antimicrobial regimens, while antimicrobial stewardship demands rapid de-escalation when possible, as soon as the susceptibility of the infectious agent is determined. Accordingly, obtaining a reliable same-shift antibiotic susceptibility profile is desired. Here we assess the performance of the CE-marked SPECIFIC REVEAL Rapid AST System (Specific Diagnostics) on GN bacteremia samples obtained in 6 leading hospitals across France and England, comparing its accuracy to the existing standard of care.

Study Design

Prospective blood cultures positive with Gram-negative bacteria were collected across 5 hospitals in France and England in 2021. In addition, 200 representative *P. aeruginosa* isolates from the French National Repository were tested at the 6th hospital using contrived blood cultures. REVEAL performance was assessed against the standard of care method and interpreted using EUCAST/CA-SFM breakpoints.

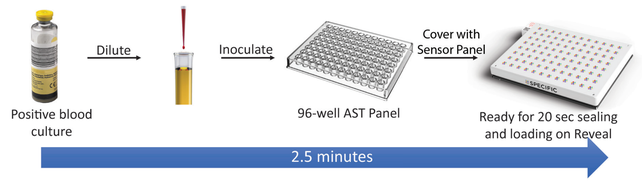
The SPECIFIC REVEAL Technology

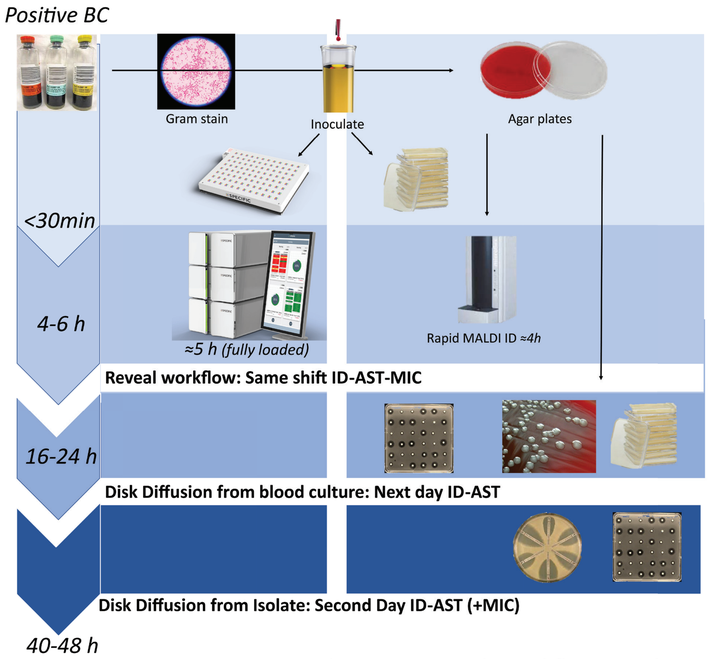
An array of 96 7-indicator nanoporous printed volatile sensor arrays are positioned above each well of a 96-well antibiotic plate. Changes in sensor color produced by the volatile emissions associated with microbial growth are used to measure population growth and hence antimicrobial effectiveness in each well. Sensor color is monitored every 10 minutes by line scan, producing 21 (7 sensors x R, G and B color channels), with one such plot in the figure below.



Sensor responses to the positive (no drug) control (black trace) and negative control (no growth medium) (flat yellow trace) are compared to those of wells with a range of meropenem concentrations to determine the MIC. Note that growth (divergence between positive and negative control) of this MDR strain is clear at 3 hours. The lowest concentration effective at suppressing the color change indicating growth was 4 µg/mL (green trace), matching the reference MIC.

< 3-minute low-skill sample prep workflow





Reveal vs Current Disk Workflow Timelines

Study Sites and Samples Collected

Hospital	Country	Reference Method	Sample Type	# of Samples	%R
Hôpital Raymond-Poincaré	France	Direct Disk Diffusion	Clinical Bacteremia	101	23.0
Kremlin-Bicêtre	France	Direct Disk Diffusion	Clinical Bacteremia	100	19.7
CHU Rennes	France	Direct Disk Diffusion	Clinical Bacteremia	103	12.5
Hôpital Avicenne	France	Direct Disk Diffusion	Clinical Bacteremia	98	15.7
HSL, London	UK	BD-Phoenix	Clinical Bacteremia	95	14.1
CHRU, Besançon	France	Thermo Scientific Sensititre	Spiked *P. aeruginosa*	200	36.6

Results

Samples Collected and SPECIFIC REVEAL Performance

Overall performance of REVEAL AST across all sites	
Categorical agreement (CA)	96.7%
Minor Errors (mE)	2.6% (252 / 9566)
Major Errors (ME)	0.75% (49 / 6576)
Very Major Errors (VME)	0.79% (16 / 2031)
Average time to result	5h 36 min

Species	Number
E. coli	249
K. pneumoniae	94
P. aeruginosa	68 (+200)
E. cloacae	45
K. aerogenes	16
K. oxytoca	11
C. koseri	9

SPECIFIC REVEAL Performance by Antimicrobial Agent

Antibiotic	#S	#I	#R	Total	TTR	#CA	#mE	#ME	#VME	CA
Amikacin	628	8	52	688	5h 15min	673	11	4	1	97.67%
Ampicillin	37	0	60	97	4h 30min	97	0	0	0	100.00%
Aztreonam	355	17	85	457	5h 36min	434	16	8	0	94.75%
Cefazolin	0	0	15	15	5h 13min	15	0	0	0	100.00%
Cefepime	379	131	176	686	5h 55min	646	37	3	1	94.10%
Cefotaxime	251	7	80	338	5h 59min	328	7	3	0	97.04%
Cefoxitin	347	1	9	357	5h 13min	353	2	2	0	98.88%
Ceftazidime	366	129	192	687	5h 59min	663	23	1	0	96.36%
Ceftazidime_Avibactam	287	0	24	311	6h 04min	306	0	3	2	98.39%
Ceftolozane_Tazobactam	186	0	46	232	6h 25min	229	0	1	2	98.71%
Cefuroxime	100	61	43	204	4h 56min	203	1	0	0	99.51%
Ciprofloxacin	310	122	173	605	5h 24min	576	21	9	0	95.04%
Ertapenem	415	4	4	423	6h 15min	419	4	0	0	99.05%
Gentamicin	413	1	67	481	5h 53min	479	1	2	0	99.38%
Imipenem	372	129	93	594	6h 18min	576	17	0	1	96.97%
Levofloxacin	227	121	150	498	5h 46min	484	14	0	1	96.99%
Meropenem	492	59	37	588	6h 18min	562	27	0	0	95.49%
Nitrofurantoin	39	0	1	40	6h 28min	40	0	0	0	100.00%
Piperacillin	161	7	308	476	4h 27min	466	5	6	0	97.69%
Piperacillin_Tazobactam	374	143	151	668	6h 33min	610	52	1	6	91.17%
Tobramycin	551	8	132	691	5h 08min	682	9	1	0	98.55%
Co-Trimoxazole	281	5	133	419	4h 36min	407	5	5	2	97.14%

Conclusion

Across ~700 samples from 6 hospital laboratories in France and England, overall categorical agreement was 96.7%, and very major error just 0.8% despite a high degree of resistant samples. Results were available in an average of 5.5 hours across all strains and antibiotics, with each antibiotic averaging between 4.5 to 6.5 hours. All antibiotics had overall categorical agreement of >94.0% with the exception of piperacillin/tazobactam which had a CA of 91.2%. However, most CA errors for piperacillin/tazobactam were minor errors. We conclude that the SPECIFIC REVEAL Rapid AST System allows the reliable same-shift determination of MIC directly from a positive blood culture.