VITEK® REVEAL™

Quantitative AST of Blood Cultures using Small Molecule Sensor Array Technology

ICD-10 Coordination and Management Committee Meeting
March 19, 2024

BACKGROUND ON BLOODSTREAM INFECTIONS

- Bloodstream infections (BSIs) refer to the presence of viable bacterial or fungal pathogens in the bloodstream that elicit an inflammatory response in patients

- BSI can be primary or secondary (i.e., secondary to an infection at another body site (e.g., surgical site infection, urinary tract infection)) and are most commonly caused by bacterial pathogens
  - Substantial portion of BSIs are caused by Gram-negative bacteria
  - Most frequent causative agents for Gram-negative BSIs are *E. coli*, *K. pneumoniae*, and *P. aeruginosa*

- Between 2000 – 2015, the incidence of BSI in developed countries in Europe and North America was 113 – 220 per 100,000 people.[1]
  - Estimated 280,000 BSI in the U.S. caused by Gram-negative bacteria[2]

- BSIs can lead to sepsis, a life-threatening condition caused by a dysregulated host response to infection that results in organ dysfunction
  - In a typical year, 1.7 million adults in the US develop sepsis and 350,000 patients with sepsis die during their hospitalization[3]

1 Kern WV, Rieg S. Burden of bacterial bloodstream infection-a brief update on epidemiology and significance of multidrug-resistant pathogens. *Clin Microbiol Infect*. 2020;26(2):151-157.
2 Al-Hasan MN. Gram-Negative Bloodstream Infection: Implications of Antimicrobial Resistance on Clinical Outcomes and Therapy. *Antibiotics (Basel)*. 2020;9(12).
3 Rhee C, Jones TM, Hamad Y, et al. Prevalence, Underlying Causes, and Preventability of Sepsis-Associated Mortality in US Acute Care Hospitals. *JAMA Netw Open*. 2019 Feb; 2(2): e187571.

WITH SEPSIS, TIME IS OF THE ESSENCE

Sepsis is a life-threatening condition that occurs when the body's response to infection damages its own organs—especially if not recognized early and treated promptly.

- Sepsis is the leading cause of death in hospitals.[1]
- 1 in 3 patients who dies in a hospital has sepsis.[2]
- 47 million cases of sepsis occur each year
  Every 2.8 seconds someone dies from sepsis.[3]
- Risk of dying increases for every hour treatment is delayed.[4]
- The cost per hospital stay is double the average cost per stay across all other conditions.[5]

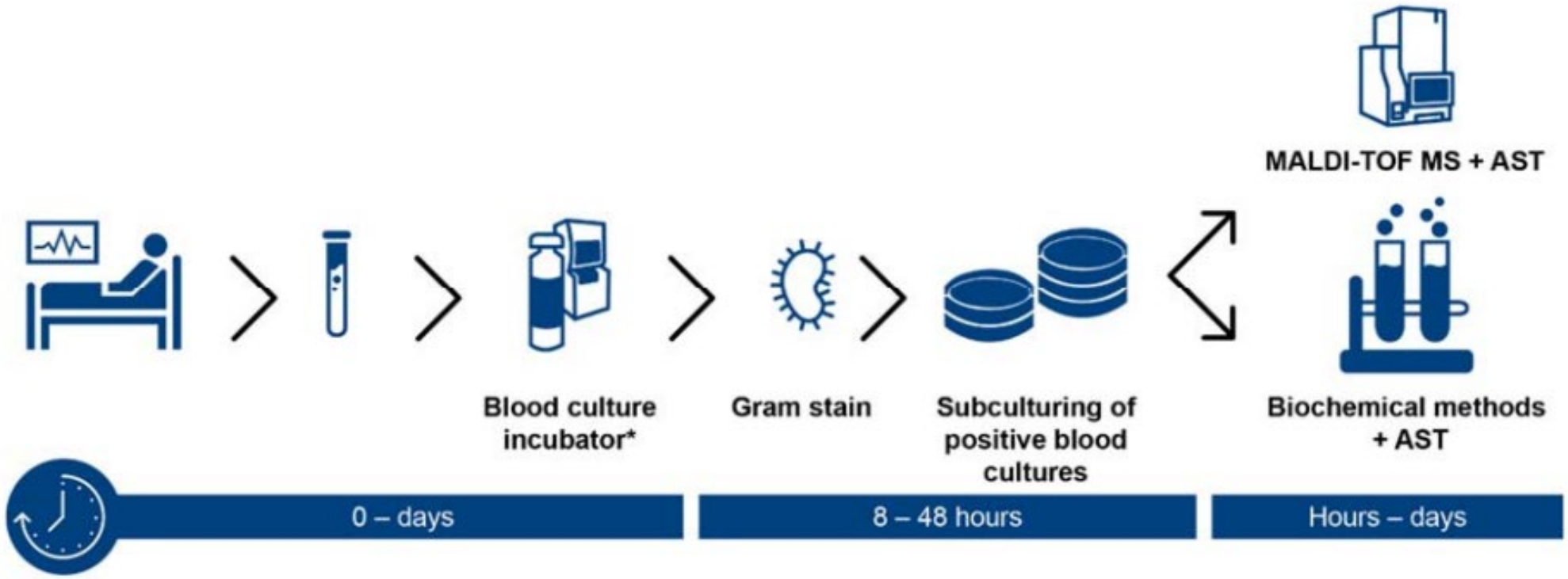
1 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32989-7/fulltext
2 https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_final_report_EN.pdf?ua=1
3 https://www.cdc.gov/sepsis/clinicaltools/index.html
4 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5649973/.
5 https://www.ncbi.nlm.nih.gov/books/NBK121966/

TIMELY AND PATHOGEN-DIRECTED TREATMENT

- Need for timely and pathogen-directed treatment for BSIs consistent with international recommendations for sepsis
  - Suppressing the underlying bacterial infection is a main early objective in the treatment
- Surviving Sepsis Campaign (SSC) guidelines recommend for empiric broad-spectrum antimicrobials to be initiated within one hour of suspected septic shock or sepsis in order to avoid poor clinical outcomes associated with delayed treatments[1]
  - Given the inability to diagnose BSI (or sepsis-causing) pathogens in that short period of time, a broad-spectrum antimicrobial treatment approach is probabilistic in nature
- However, broad-spectrum empiric antibiotic therapy is inappropriate in at least 30% of the patients, and over-treatment or under-treatment of an underlying bacterial infection is linked to its own issues[2,3]
- Empiric therapy needs to be adjusted as quickly as bacterial pathogens and their antibiotic resistance patterns are identified

1 Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. Crit Care Med. 2021;49(11):e1063-e1143.
2 Marquet K, Liesenborgs A, Bergs J, Vleugels A, Claes N. Incidence and outcome of inappropriate in-hospital empiric antibiotics for severe infection: a systematic review and meta-analysis. *Crit Care*. 2015;19(1):63.
3 Zhang D, Micek ST, Kollef MH. Time to Appropriate Antibiotic Therapy Is an Independent Determinant of Postinfection ICU and Hospital Lengths of Stay in Patients With Sepsis. *Crit Care Med*. 2015;43(10):2133-2140.

TRADITIONAL DIAGNOSTIC PATHWAY



Blood cultures are performed with continuous monitoring blood culture systems which detect the growth of microorganisms based on the emission of carbon dioxide during microbial metabolism. Blood cultures are incubated for up to 5 days, with microorganisms typically detected within 24–48 hours.

OVERVIEW OF VITEK® REVEAL™ RAPID AST TECHNOLOGY*

- Innovative technology – Received breakthrough device designation by the FDA
- Timely – Results in an average of 5.5 hours and intended to be used in conjunction with Gram stain, organism identification, and other clinical laboratory findings
  - Faster turnaround time to clinically important results of a positive blood culture, enabling faster changes in antibiotic therapy
    - Support faster antimicrobial therapy as necessary
    - Timely de-escalation in cases with unnecessary broad-spectrum antimicrobial administration
- Sample – Positive blood cultures (PBC) due to clinically validated Gram-negative organisms
- Results – Provides minimum inhibitory concentrations and interpretive categories for pathogen-antibiotic combinations
  - Interpretive categories
    - Susceptible (S)
    - Intermediate (I)
    - Resistant (R)

* VITEK® REVEAL™ Rapid AST System is pending FDA clearance and not available for sale in the US

OVERVIEW OF VITEK® REVEAL™ RAPID AST SYSTEM*

FAST
FROM POSITIVE BC, RESULTS IN AN AVERAGE OF 5.5H

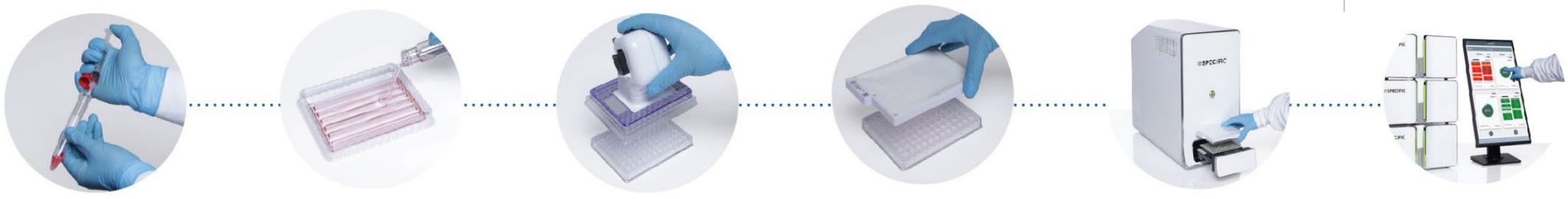
ACTIONABLE
WIDE ANTIMICROBIAL COVERAGE
FOR BLOODSTREAM GRAM NEGATIVE INFECTION

INTEGRATED
WITHIN THE BIOMÉRIEUX SEPSIS SOLUTION

* VITEK® REVEAL™ Rapid AST System is pending FDA clearance and not available for sale in the US

WORKFLOW FOR VITEK® REVEAL™ RAPID AST SYSTEM*

Sample Prep in <3 Minutes



Average 5.5 Hours Time to Result

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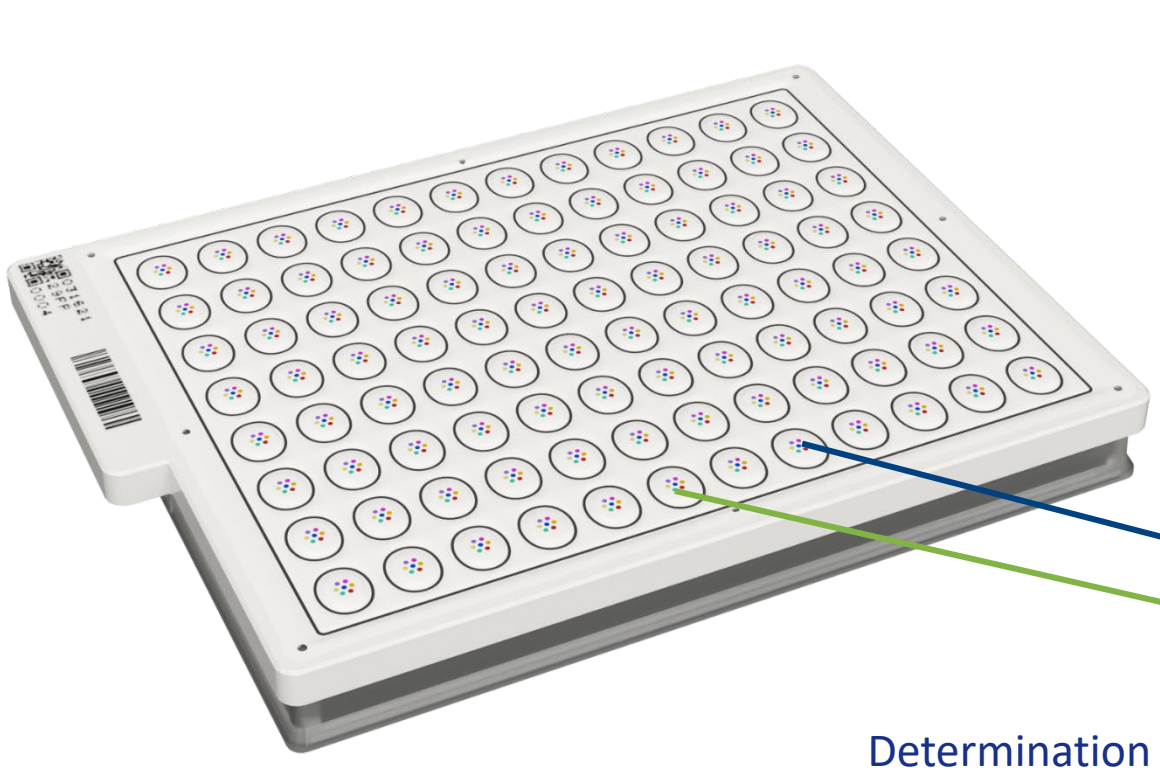
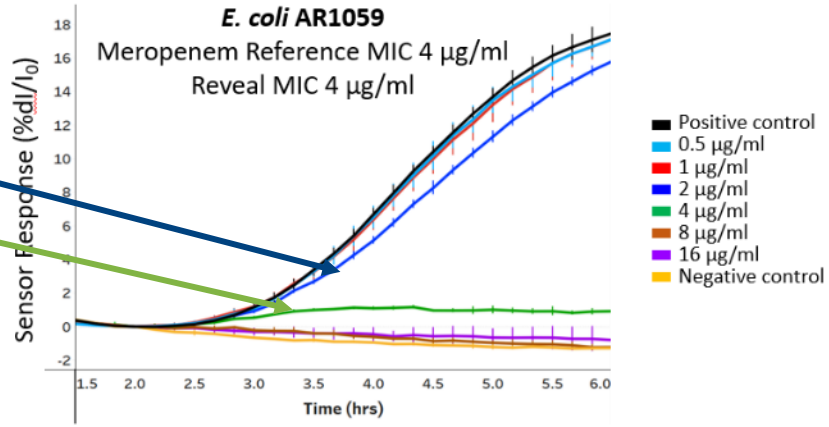
VITEK® REVEAL™ SMALL MOLECULE SENSOR ARRAY

Each sensor generates a colorimetric reaction to the metabolic volatiles (volatile organic compounds, VOCs) released by microorganisms during growth



Determination of MIC's

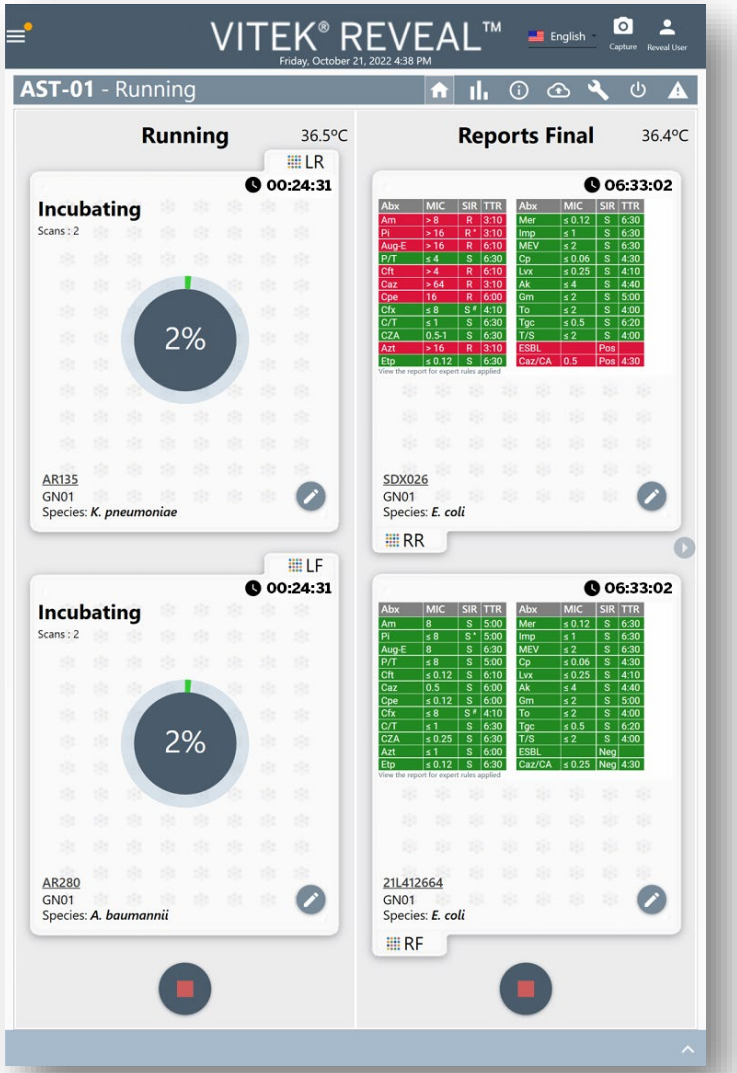


VITEK® REVEAL™ SOFTWARE

Intuitive, touchscreen user interface for users

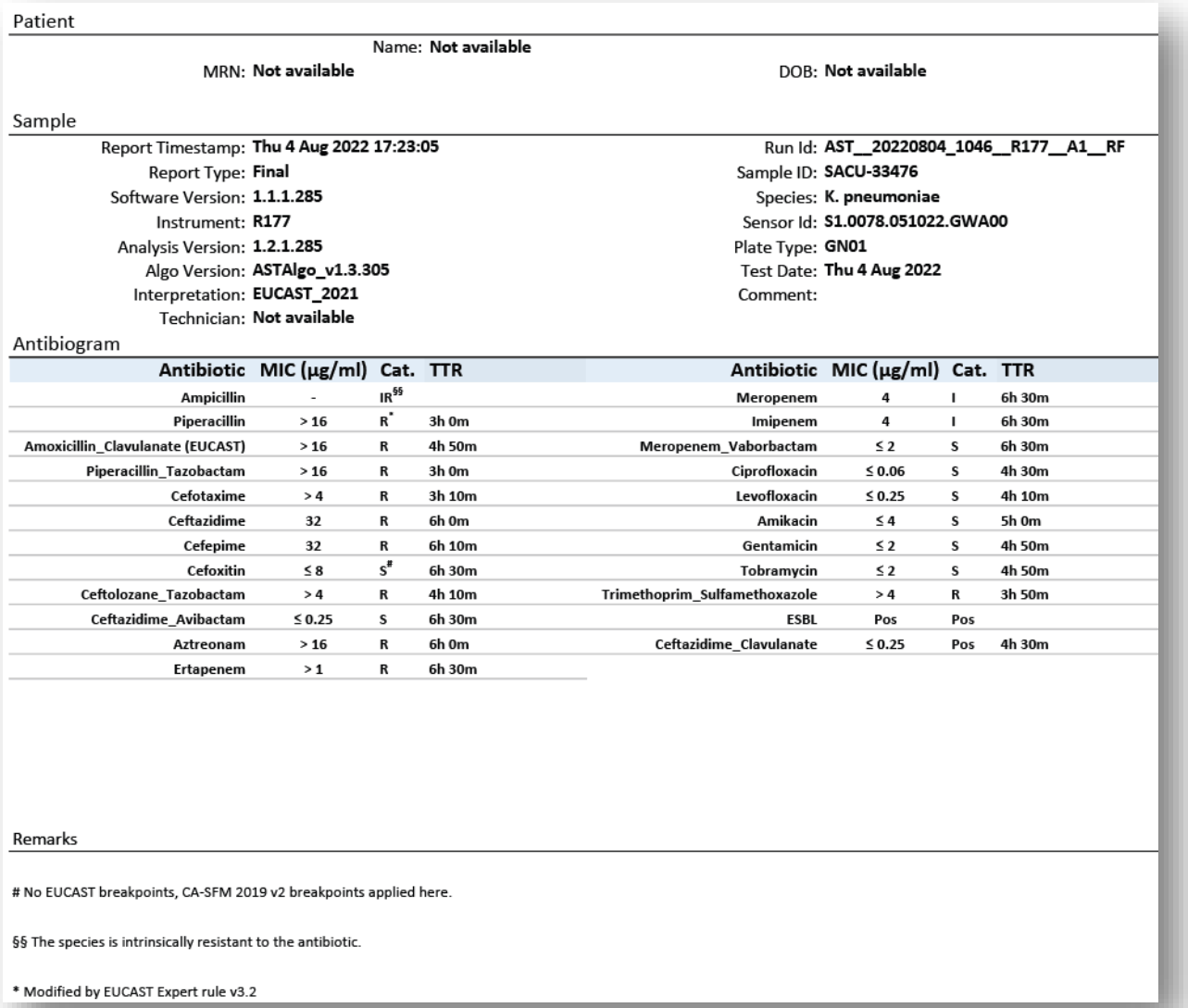
Real-time Monitoring of MIC's and Interpretation

- The software generates AST results in real time.
- The first AST results as early as **3.5 hours.**



DOCUMENTATION

- Findings from the antimicrobial susceptibility testing will be sent to the laboratory information system
- The approach for documenting the procedure in the medical record will vary by provider
  - Possible terms to describe the use of the system: VITEK® REVEAL™ Rapid AST System, VITEK® REVEAL™ AST System, VITEK® REVEAL™, or AST
- Documentation Example
  - Notes AST in the medical record under Laboratory results, Microbiology, either with the Positive Blood Culture result or under Susceptibility



Patient

Name: **Not available**

MRN: **Not available** DOB: **Not available**

Sample

Report Timestamp:	**Thu 4 Aug 2022 17:23:05**	Run Id:	**AST__20220804_1046__R177__A1__RF**
Report Type:	**Final**	Sample ID:	**SACU-33476**
Software Version:	**1.1.1.285**	Species:	**K. pneumoniae**
Instrument:	**R177**	Sensor Id:	**S1.0078.051022.GWA00**
Analysis Version:	**1.2.1.285**	Plate Type:	**GN01**
Algo Version:	**ASTAlgo_v1.3.305**	Test Date:	**Thu 4 Aug 2022**
Interpretation:	**EUCAST_2021**	Comment:	
Technician:	**Not available**		

Antibiogram

Antibiotic	MIC (µg/ml)	Cat.	TTR	Antibiotic	MIC (µg/ml)	Cat.	TTR
Ampicillin	-	IR§§		Meropenem	4	I	6h 30m
Piperacillin	> 16	R*	3h 0m	Imipenem	4	I	6h 30m
Amoxicillin_Clavulanate (EUCAST)	> 16	R	4h 50m	Meropenem_Vaborbactam	≤ 2	S	6h 30m
Piperacillin_Tazobactam	> 16	R	3h 0m	Ciprofloxacin	≤ 0.06	S	4h 30m
Cefotaxime	> 4	R	3h 10m	Levofloxacin	≤ 0.25	S	4h 10m
Ceftazidime	32	R	6h 0m	Amikacin	≤ 4	S	5h 0m
Cefepime	32	R	6h 10m	Gentamicin	≤ 2	S	4h 50m
Cefoxitin	≤ 8	S#	6h 30m	Tobramycin	≤ 2	S	4h 50m
Ceftolozane_Tazobactam	> 4	R	4h 10m	Trimethoprim_Sulfamethoxazole	> 4	R	3h 50m
Ceftazidime_Avibactam	≤ 0.25	S	6h 30m	ESBL	Pos	Pos	
Aztreonam	> 16	R	6h 0m	Ceftazidime_Clavulanate	≤ 0.25	Pos	4h 30m
Ertapenem	> 1	R	6h 30m				

Remarks

No EUCAST breakpoints, CA-SFM 2019 v2 breakpoints applied here.

§§ The species is intrinsically resistant to the antibiotic.

* Modified by EUCAST Expert rule v3.2

SUMMARY

- VITEK® REVEAL™ Rapid AST System is a breakthrough designated device that is pending FDA clearance.
  - bioMérieux has applied for NTAP for VITEK® REVEAL™ Rapid AST System as part of the FY 2025 cycle.
- Proposed indication*: The VITEK® REVEAL™ Rapid AST System is an *in vitro* diagnostic (IVD) automated system for quantitative and qualitative antimicrobial susceptibility testing (AST) of organisms direct from positive blood culture. The VITEK® REVEAL™ GN AST Assay is indicated for susceptibility testing of clinically validated Gram-negative pathogenic bacteria commonly associated with or causing bacteremia. This test predicts patient response to antimicrobials and is performed by laboratory health professionals in a clinical diagnostic setting. Results are intended to be used in conjunction with Gram stain, organism identification, and other clinical laboratory findings.
- There is no existing code that accurately describes the VITEK® REVEAL™ Rapid AST System. Thus, bioMérieux requests the creation of a new ICD-10-PCS code that describes this type of technology.

* Pending FDA clearance; subject to change