MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

Plan Nacional Resistencia Antibióticos

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I Jornada del Comité Español del Antibiograma (COESANT)

Madrid 24 de noviembre de 2022

Técnicas rápidas de estudio de sensibilidad antibiótica

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¿Por qué debemos generar resultados rápidos de sensibilidad antibiótica?

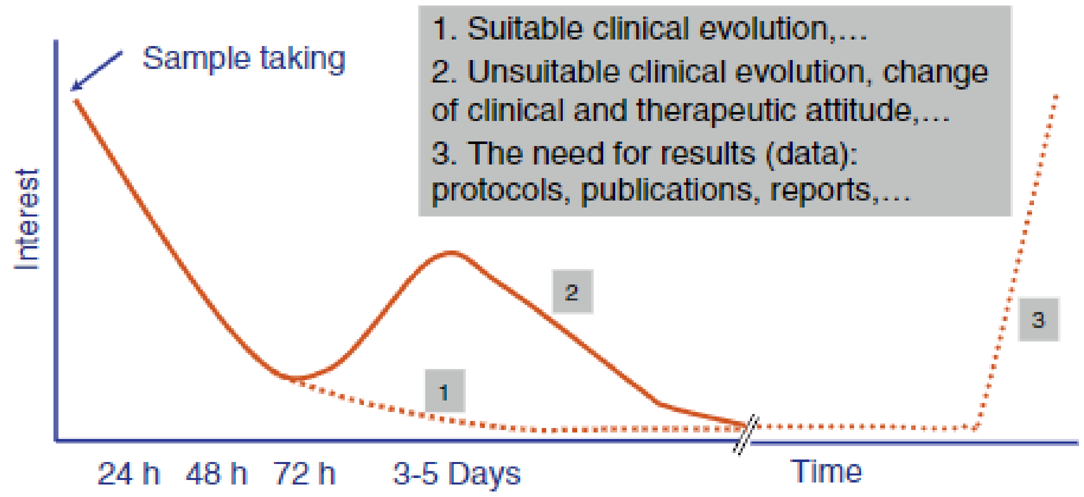

Figure 1. Evolution of the interest in the results of microbiological studies by the doctor who requested them.

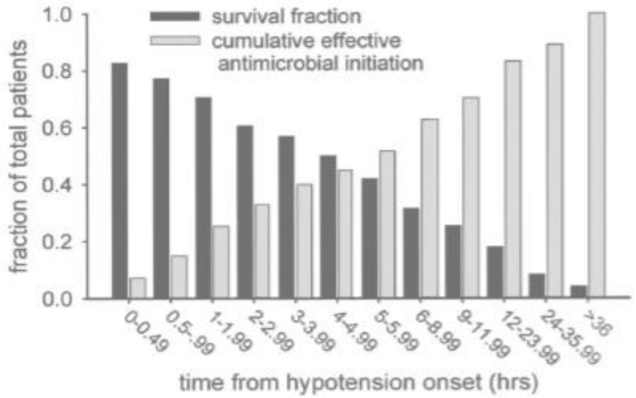

Figure 1. Cumulative effective antimicrobial initiation following onset of septic shock-associated hypotension and associated survival. The x-axis represents time (hrs) following first documentation of septic shock-associated hypotension. *Black bars* represent the fraction of patients surviving to hospital discharge for effective therapy initiated within the given time interval. The *gray bars* represent the cumulative fraction of patients having received effective antimicrobials at any given time point.

Cantón R, Gómez G de la Pedrosa E. Economic impact of rapid diagnostic methods in Clinical Microbiology: Price of the test or overall clinical impact. Enferm Infecc Microbiol Clin. 2017 Dec;35(10):659-666.

Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, Suppes R, Feinstein D, Zanotti S, Taiberg L, Gurka D, Kumar A, Cheang M. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006 Jun;34(6):1589-96.

¿Por qué debemos generar resultados rápidos de sensibilidad antibiótica?

- Antibiogramas rápidos

- Mejoran eficacia clínica – reducción de mortalidad y complicaciones infecciosas
- Favorecen el "antibiotic stewadship"
- Optimizan la toma de medidas de control de la infección

¿Qué consideramos un resultado rápido de sensibilidad antibiótica?

Hay muchas opiniones sobre lo que constituye una "AST rápida", pero la mayoría de los microbiólogos clínicos definen la prueba rápida como **factible durante un solo turno de trabajo**, es decir, dentro de las 8 horas o menos.

van Belkum A, Burnham CD, Rossen JWA, Mallard F, Rochas O, Dunne WM Jr. Innovative and rapid antimicrobial susceptibility testing systems. Nat Rev Microbiol. 2020 May;18(5):299-311.

Factores a tener en cuenta para un antibiograma rápido

- Fase preanalítica	- Correcto flujo de petición/envío de muestras - Atención continuada en el laboratorio - Selección de muestra/paciente a realizar la prueba
- Fase analítica	- Antibiogramas directos - Lectura rápida con antibiogramas convencionales - Nuevas técnicas de antibiogramas rápidos
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Antibiogramas directos

Muestra

Hemocultivos

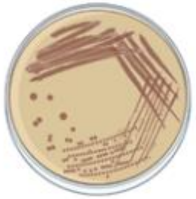
Aspirados traqueobronquiales

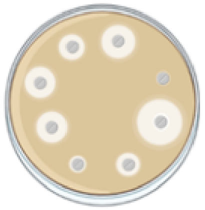
Orinas

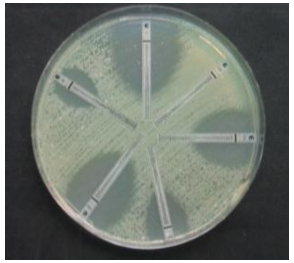
Otras

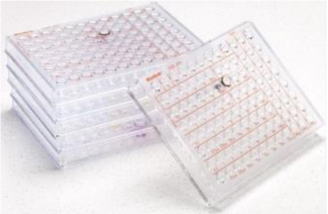
★

Con o sin preprocesamiento









Quirino A, Marascio N, Peronace C, Gallo L, Barreca GS, Giancotti A, Lamberti AG, Colosimo M, Minchella P, Trecarichi EM, Torti C, Liberto MC, Matera G. Direct antimicrobial susceptibility testing (AST) from positive blood cultures using Microscan system for early detection of bacterial resistance phenotypes. Diagn Microbiol Infect Dis. 2021 Oct;101(2):115485.

Hogan CA, Watz N, Budvytiene I, Banaei N. Rapid antimicrobial susceptibility testing by VITEK®2 directly from blood cultures in patients with Gram-negative rod bacteremia. Diagn Microbiol Infect Dis. 2019 Jun;94(2):116-121.

Åkerlund A, Jonasson E, Matuschek E, Serrander L, Sundqvist M, Kahlmeter G; RAST Study Group. EUCAST rapid antimicrobial susceptibility testing (RAST) in blood cultures: validation in 55 European laboratories. J Antimicrob Chemother. 2020 Nov 1;75(11):3230-3238.

Torres-Sangiao E, Lamas Rodriguez B, Cea Pájaro M, Carracedo Montero R, Parajó Pazos N, García-Riestra C. Direct Urine Resistance Detection Using VITEK 2. Antibiotics (Basel). 2022 May 15;11(5):663.

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European Committee on Antimicrobial Susceptibility Testing

Zone diameter breakpoint tables for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles

Version 5.1, valid from 2022-05-02

This document should be cited as "The European Committee on Antimicrobial Susceptibility Testing. Zone diameter Breakpoint Tables for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles. Version 5.1, 2022. http://www.eucast.org."

Content	Page	Additional information
Changes	1	
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Guidance on reading EUCAST RAST Breakpoint Tables	4	
Information on technical uncertainty	5	
Escherichia coli	6	Breakpoints for 4, 6, 8 and 16-20 h
Klebsiella pneumoniae	7	Breakpoints for 4, 6, 8 and 16-20 h
Pseudomonas aeruginosa	8	Breakpoints for 6, 8 and 16-20 h
Acinetobacter baumannii	9	Breakpoints for 4, 6 and 8 h
Staphylococcus aureus	10	Breakpoints for 4, 6, 8 and 16-20 h
Enterococcus faecalis	11	Breakpoints for 4, 6 and 8 h
Enterococcus faecium	12	Breakpoints for 4, 6 and 8 h
Streptococcus pneumoniae	13	Breakpoints for 4, 6, 8 and 16-20 h

https://www.eucast.org/

Métodos de antibiograma rápidos y directos desde hemocultivo positivo

Table 4. Theoretical and actual numbers of tests, the proportions of tests that could be read and interpreted as S or R after 4, 6 and 8 h and the categorical errors with RAST versus standard DD by EUCAST breakpoint tables version 8.0 at each reading time for all species in NE + SE [RAST breakpoint table version 0 (v. 0) and version 1 (v. 1.0)]

	Incubation time (h)					
	4		6		8	
Breakpoint table	v. 0	v. 1.0	v. 0/v. 1.0		v. 0/v. 1.0	
Theoretical number of tests[a]	7024	7361	7361		7361	
Number of completed tests[b]	6398	6718	7210		6655	
Readable zones[c] (% of completed tests)	5624 (88)	5811 (87)	6921 (96)		6561 (99)	
Results calculated on readable zones (%)						
breakpoint table	v. 0	v. 1.0	v. 0	v. 1.0	v. 0	v. 1.0
not interpreted as S or R (ATU)	20	16	16	7.5	14	5.7
interpreted as S	71	75	76	84	78	86
interpreted as R	8.8	8.8	7.6	8.5	7.7	8.6
Errors calculated on the total number of zones interpreted as S or R (%)						
breakpoint table	v. 0	v. 1.0	v. 0	v. 1.0	v. 0	v. 1.0
mEs	0.7	0.6	0.5	0.6	0.6	0.8
MEs	2.2	2.1	0.9	1.1	0.7	0.9
VMEs	0.2	0.2	0.4	0.4	0.6	0.5
total errors	3.1	3.0	1.8	2.1	1.8	2.2

Total number of isolates included: *n* = 1151.
Minor error (mE; RAST = S or R and reference method = I); major error (ME; RAST = R and reference method = S); very major error (VME; RAST = S and reference method = R).
[a]Total number of possible isolate/agent combinations. The lower number of tests at 4 h (breakpoint table v. 0) is explained by the absence of norfloxacin breakpoints for *S. aureus*.
[b]Number of completed tests after excluding missing data (e.g. disc dropped).
[c]Number of tests with readable inhibition zones.

Åkerlund A, Jonasson E, Matuschek E, Serrander L, Sundqvist M, Kahlmeter G; RAST Study Group. EUCAST rapid antimicrobial susceptibility testing (RAST) in blood cultures: validation in 55 European laboratories. J Antimicrob Chemother. 2020 Nov 1;75(11):3230-3238.

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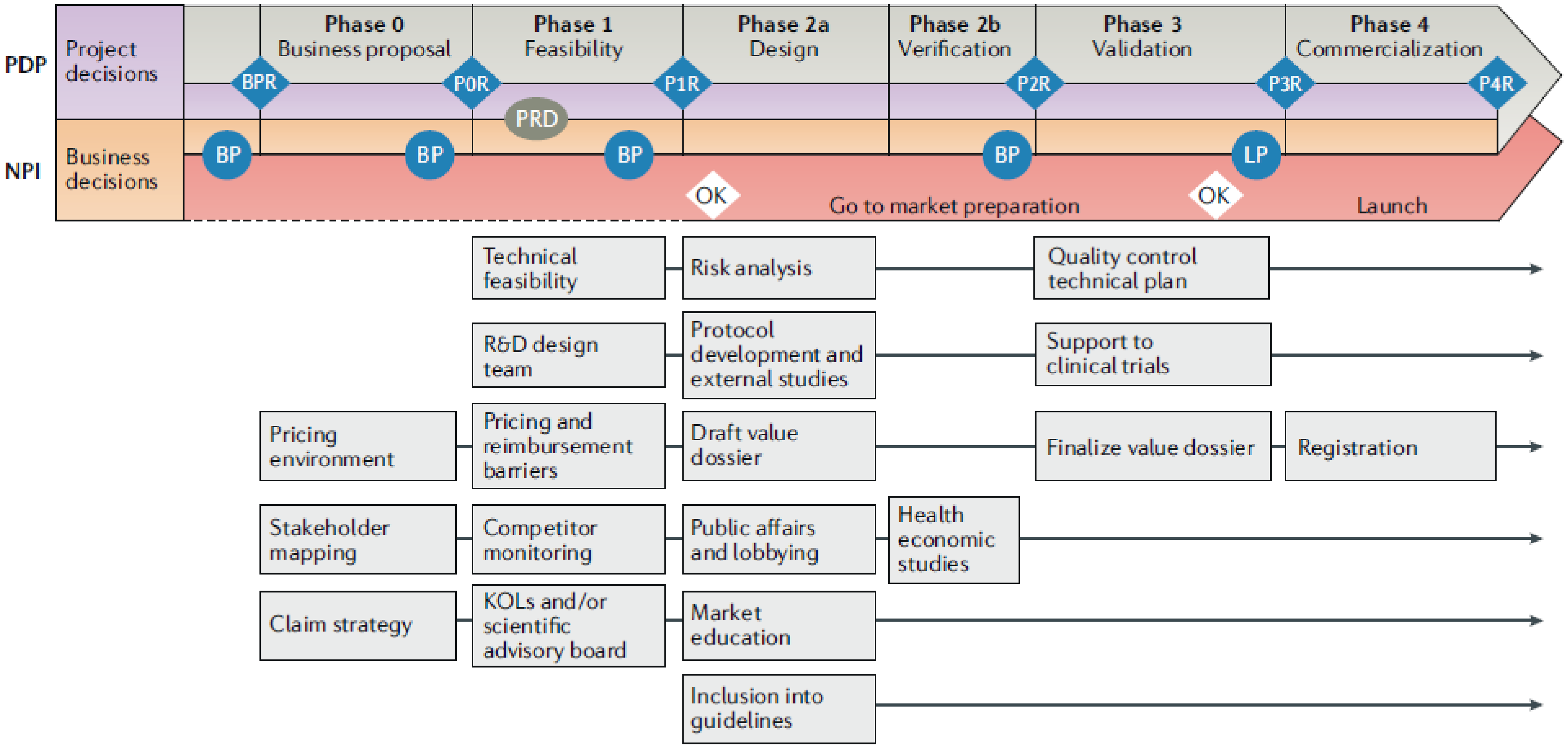
- Fase analítica

- Antibiogramas directos
- Lectura rápida con antibiogramas convencionales
- Nuevas técnicas de antibiogramas rápidos

- Fase postanalítica

- Flujo continuo de información de resultados
- Utilización de sistemas de información/alerta en dispositivos portables

Desarrollo de sistemas de evaluación de la sensibilidad a los antibióticos: hoja de ruta



an Belkum A, Bachmann TT, Lüdke G, Lisby JG, Kahlmeter G, Mohess A, Becker K, Hays JP, Woodford N, Mitsakakis K, Moran-Gilad J, Vila J, Peter H, Rex JH, Dunne WM Jr; JPIAMR AMR-RDT Working Group on Antimicrobial Resistance and Rapid Diagnostic Testing. Developmental roadmap for antimicrobial susceptibility testing systems. Nat Rev Microbiol. 2019 Jan;17(1):51-62.

Métodos rápidos para la determinación de la sensibilidad a los antibióticos

- Métodos detección mecanismos de resistencia

- Moleculares (RT-PCR, LAMP. NGS, etc…)
- Fenotípicos (colorimétricos, inmunocromatográficos, etc…)
- MALDI-TOF MS

- Métodos fenotípicos para la realización de antibiogramas rápidos

Microbiological parameters
• One versus many cells
• One versus more species
• Heterogeneous AMR
• Cell permeability
• Metabolic status
• Rapid versus slow growth
• Induction of resistance
• Low-level resistance
• New resistance mechanism

Toolbox	Read-out	Suited for single cells
Microfluidics	Viability, growth	✓
Droplet test	Viability, growth	
Cytometry	Viability, growth	✓
Microscopy	Morphology	✓
Mass spectrometry	Spectral change	
Light scattering	Spectral change	
Electrochemistry	Conductivity	
Cantilevers	Viability, growth	✓
NMR	Spectral change	
Microsound	Movement	
Phages	Viability, growth	
Calorimetrics	Viability, growth	
Transcriptomics	Viability, growth	✓

van Belkum A, Burnham CD, Rossen JWA, Mallard F, Rochas O, Dunne WM Jr. Innovative and rapid antimicrobial susceptibility testing systems. Nat Rev Microbiol. 2020 May;18(5):299-311.

- Métodos basados en antibiograma molecular

Nuevos métodos para la determinación de la resistencia a los antibióticos

Table 1 | **New offers in qualitative and quantitative AST systems**

Companies[a]	Technologies used	Approach and system	Country of origin	Status
Abacus Diagnostica	PCR platform; portfolio includes methicillin-resistant *Staphylococcus aureus* and *Clostridioides difficile*	Molecular; Genomera CDX	Finland	Developed in 2012
Affinity Biosensors	Microorganism mass measurement	Phenotypic; LifeScale AST	USA	Sold since 2017 but unavailable in the USA
Arc Bio	Identification and AST based on shotgun sequencing	Genomic; Galileo pathogen solution	USA	Launched in 2018
ARCDIA International Oy Ltd	mariAST measures species-specific bacterial growth in real time and combines in-well culture and high-accuracy detection	Phenotypic; mariPOC	Finland	In approval process
ARES Genetics	Development of AST database and currently developing an associated wet laboratory approach	Genomic; bioinformatics; GEAR database	Austria	Established in 2017
Ascenion GmBH	Combination of a BacLight viability staining with automated confocal laser scanning microscopy and detailed image analysis	Phenotypic; autofocus microscopy	Germany	Patent registered in 2010; the technology is offered for in-licensing or co-development of a screening platform
AUS Diagnostics	Multiplexed tandem PCR	Molecular; Mini- and UltraPlex	Australia	Sold since 2018, European conformity marking announced
BacterioScan	Laser light-scattering instrument	Phenotypic; 216 Dx urinary tract infection (UTI) system	USA	In 2018 the FDA issued a 510K premarket notification clearance for the 216Dx UTI detection system
BioFire	Multiplexed, syndrome-oriented PCR	Molecular; FilmArray	USA	Various tests cleared for sale by the FDA
Biotrack Diagnostics	Solid-state cytometry or fluorescence in situ hybridization and specific antibodies for fluorescent micro-agglutination are used for specific detection of molecules	Phenotypic; biochemical; AquaScope and AquaPrep	The Netherlands	Not known
Click Diagnostics	Cartridge-based, hand-held thermocyclers configured to move a fluid between distinct chambers and visually read colorimetric results	Molecular; company in stealth mode	USA	Not known
Dayzero Diagnostics	High-throughput bacterial DNA sequencing and proprietary machine-learning algorithms to rapidly predict pathogen species and drug resistance profiles	Genomic; bioinformatics; epiXact	USA	In development since March 2018
EliTech Group	Triplex PCR assay	Molecular; URIFAST	France	Sold since 2018
FASTinov	Cell sorting	Cellular detection, FACS	Portugal	Patent available since 2012, no products to date
Firebird	Molecularly targeted nucleic acid testing	Molecular; next-generation DNA sequencing	US	Not known
First Light Biosciences	Offers sensitive detection of diagnostic markers directly in complex sample matrices	Molecular; MultiPath platform	USA	Presented at the American Society for Microbiology conference in 2019
GeneCapture	Non-amplified RNA detection	Molecular; CAPTURE platform	USA	Early development; POC platform estimated date of launch, 2025
GeneFluidics	Molecular-based, PCR-less identification of species-specific phenotypic markers of resistance and susceptibility, as they are clinically relevant end products of many genetic pathways	Molecular; UTImax	USA	Sold for research use only since December 2017
GFC Diagnostics Ltd	DNA hybridization technology and have developed a rapid, POC test for detection of MRSA	Molecular; SafeTube IsoScreen	UK	Product announced in October 2017
Gradientech AB	Proprietary microfluidic technology solution to create stable substance gradients for AST of positive blood culture samples in 2 h	Phenotypic; QuickMIC and CellDirector	Sweden	Product estimated date of launch, 2023

Table 1 (cont.) | **New offers in qualitative and quantitative AST systems**

Companies[a]	Technologies used	Approach and system	Country of origin	Status
Klaris Diagnostics (Pattern)	Uses deep neural networks to recognize the unique 'biometric fingerprint' produced by different bacterial species encapsulated within microfluidic droplets	Phenotypic; bioinformatic; single-cell biometric analysis	US	Not known
MicrobeDx Inc	Hybridization and capture of target ribosomal RNA, thus leveraging its natural amplification and negating the need for PCR	Molecular; UMD SelectNA	Germany	Product estimated date of launch, 2024
Nanopore Diagnostics LLC	iNDxer, which is a nanopore sensor for counting dilute amounts of nucleic acid biomarkers (for example, DNA, RNA) directly in minimally processed samples	Molecular; iNDxer	USA	Product estimated date of launch, 2024
Nexogen Inc	Programmable enrichment and real-time selective sequencing method for the rapid diagnostics for AMR	Molecular; not defined	USA	Prototype phase
Next Gen Diagnostics	Overnight whole-genome sequencing with bioinformatics assessment	Genomic; bioinformatics; proprietary bio-info dashboard	UK and USA	Not known
Orbital diagnostics	Scattered light integrated collector	Phenotypic; scattered light integration collector	UK	Not known
Phase Genomics	High-throughput chromatin conformation proximity ligation technology	Molecular; next-generation DNA sequencing	USA	Proof of concept published in 2017; product launch currently not known
PhAST Diagnostics	Single-cell imaging	Phenotypic system	USA	Not known
QSM Diagnostics, Inc.	Quantitative electrochemical measurement of bacterial colonization levels	Phenotypic system	USA	Not known
Resistell	Nanomotion detection-based antibiotic susceptibility testing	Phenotypic; atomic force microscopy and cantilevers	Switzerland	Not known
Selux Diagnostics	Europium-cryptate-diamine chelate used to universally label the bacterial surface; cryptates and cryptands form 3D structures that function as ion cages	Phenotypic; biochemical; bacterial surface area chemistry, next-generation phenotyping	USA	Product estimated date of launch, 2023
Seraph Biosciences Inc.	Field portable ultra-high sensitive Raman system	Phenotypic; SeraSpec	USA	Not known
Specific Diagnostics LLC	Small molecule sensor array responds to metabolic by-products and detects volatile organic compounds	Biochemical; reveal system	USA	Product estimated date of launch, 2022
Spectromics	Spectrometric monitoring of phenotypic changes that occur in reactions between the sample and a panel of candidate antibiotics	Phenotypic; 10-min POC test at the general practitioner	UK	Not known
Spindiag GmBH	Ultrafast and highly sensitive PCR for drug-resistant pneumonia and sepsis	Molecular; SpindiagONE	Germany	Product estimated date of launch, 2024
Symcel Sverige AB	Label-free multichannel assay that measures the specific metabolic phenotype of cells and pathogens in real time	Phenotypic; calScreener	Sweden	Product estimated date of launch, end of 2020
Talis Biomedical Corp.	Combination of SlipChips, fluorescence and bright field real-time imaging that enables unlimited test formats in a compact platform	Phenotypic; LAMP technology	USA	Not known
TheoremDx Inc	Simultaneous protein and DNA and/or RNA assays; high-tech graphene chips combining all methods; cheap, reliable, cloud-based artificial intelligence	Proteomic; molecular; graphene rapid identification platform	USA	Product estimated date of launch, 2025

van Belkum A, Burnham CD, Rossen JWA, Mallard F, Rochas O, Dunne WM Jr. Innovative and rapid antimicrobial susceptibility testing systems. Nat Rev Microbiol. 2020 May;18(5):299-311.

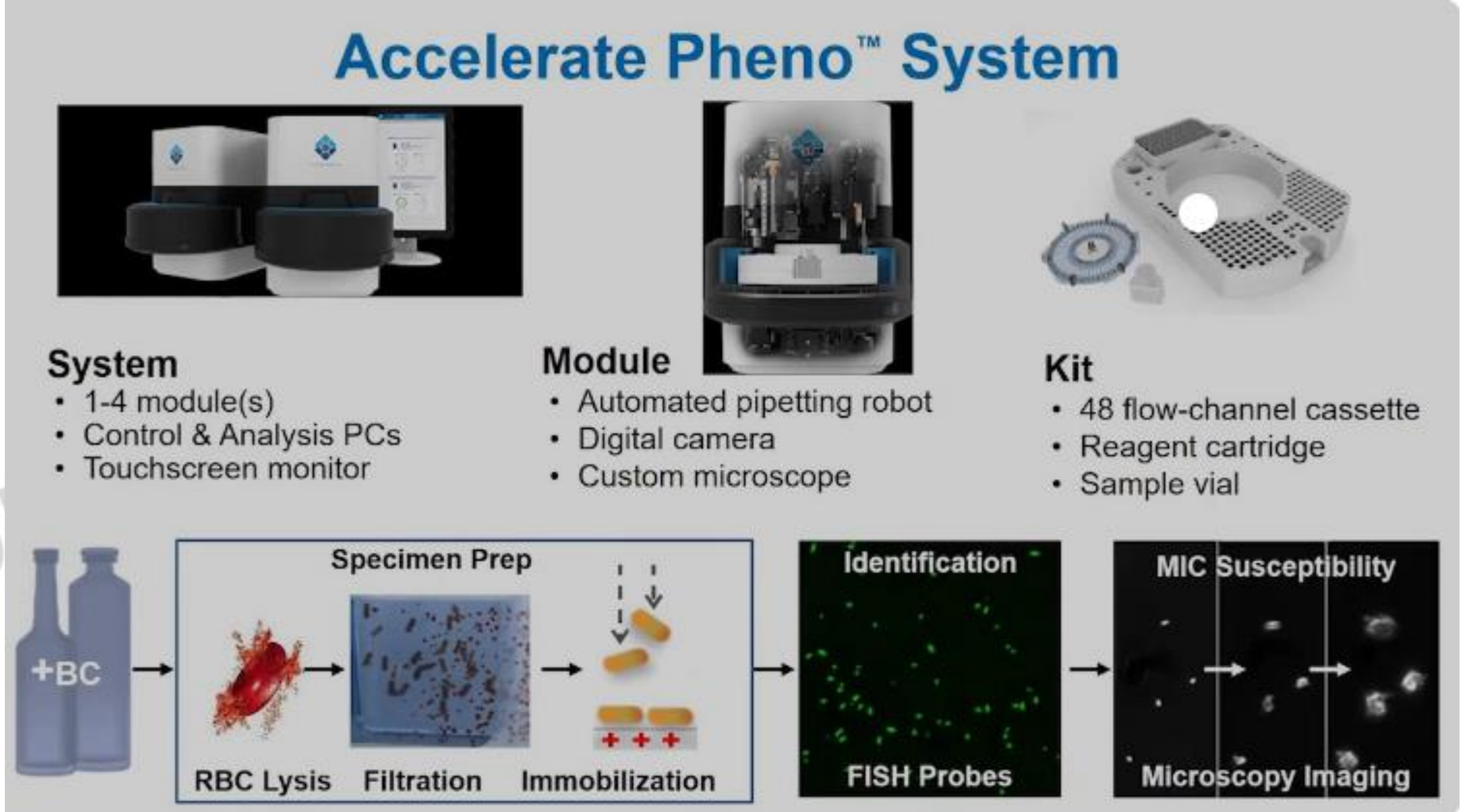
Otros métodos de antibiograma rápidos y directos desde hemocultivo positivo

Métodos AST fenotípicos rápidos aprobados para hemocultivos positivos

Técnica (casa comercial)	Tecnología	Tiempo	Aprobación
PhenoTest BC (Accelerate Diagnostics)	Microscopía FISH de campo oscuro. Se analizan los cambios morfológicos y cinéticos.	7 h	FDA
Alfred (AliFAX)	Dispersión de luz. Detección de crecimiento bacteriano en caldo de cultivo líquido.	3-5 h	CE-IVD
dRAST (QuantaMatrix)	Microscopía y análisis de imágenes de células bacterianas inmovilizadas en agarosa en microchips de plástico.	6 h	CE-IVD
Reveal AST (Specific Diagnostics)	Sensores para compuestos orgánicos volátiles emitidos durante el crecimiento de microorganismos.	4,5 h	CE-IVD
ASTar (Q-linea)	Microscopía y análisis de imágenes del crecimiento bacteriano en caldo.	3-6 h	CE-IVD
Fastinov (Fastinov)	Citometría de flujo aplicando colorantes fluorescentes que marcan daño celular ante la exposición al antibiótico.	2 h	CE-IVD
LifeScale (Affinity Biosensors)	Medida de masas mediante un microcantilever.	4 h	CE-IVD

Banerjee R, Humphries R. Rapid Antimicrobial Susceptibility Testing Methods for Blood Cultures and Their Clinical Impact. Front Med (Lausanne). 2021 Mar 10;8:635831.

Antibiogramas rápidos en hemocultivo positivo: Accelerate Pheno System



Antibiogramas rápidos en hemocultivo positivo: Accelerate Pheno System

TABLE 4 Gram-positive AST results by organism/antimicrobial combination[a]

Class or parameter	Antimicrobial agent or organism	Organism	EA (%)	CA (%)	No. of samples: Test	Fresh	Seed	No. of samples with the following AST result[b]: S	I	R	No. of errors: VME	ME	mE
Penicillins	Ampicillin	EFM	100	99	96	44	52	4	0	92	0	1	0
		EFS	100	100	142	134	8	142	0	0	0	0	0
Cephems	Ceftaroline	SAU	93.3	99.7	344	297	47	343	1	0	0	0	1
Lipopeptides	Daptomycin	SAU	98.5	99.5	197	148	49	196	0	1	1	0	0
		SLU[c]	96.6	100	29	1	28	29	0	0	0	0	0
		CoNS	100	100	135	135	0	135	0	0	0	0	0
		EFM	93	98.6	71	19	52	71	0	0	0	1	0
		EFS	100	100	40	32	8	40	0	0	0	0	0
Tetracyclines	Doxycycline[c]	SAU	96.9	97.7	383	336	47	378	5	0	0	4	5
		SLU	100	100	29	1	28	29	0	0	0	0	0
		CoNS	99.3	96.3	134	134	0	128	6	0	0	1	4
		EFM	99.2	87.1	124	69	55	83	5	36	0	0	16
Macrolides	Erythromycin	SAU	98.2	96.8	338	292	46	132	1	205	0	1	10
		SLU[c]	100	100	28	1	27	25	0	3	0	0	0
		CoNS[c]	97	95.5	134	134	0	40	1	93	1	0	5
Oxazolidinones	Linezolid	SAU	99.5	100	194	147	47	194	0	0	0	0	0
		SLU[c]	100	100	29	1	28	29	0	0	0	0	0
		CoNS[c]	100	100	135	135	0	135	0	0	0	0	0
		EFM	98.6	97.1	69	17	52	67	1	1	0	0	2
		EFS	92.7	100	41	33	8	41	0	0	0	0	0
Sulfonamide	TMP-SMX[c]	SAU	98.2	98.2	386	338	48	384	0	2	0	7	0
		SLU	89.7	89.7	29	1	28	29	0	0	0	3	0
Glycopeptide	Vancomycin	SAU	98	99	198	148	50	196	2	0	0	0	2
		SLU	100	100	29	1	28	29	0	0	0	0	0
		CoNS	100	100	134	134	0	134	0	0	0	0	0
		EFM	90.1	90.1	71	19	52	16	0	55	0	0	7
		EFS	92.7	92.7	41	33	8	36	0	5	0	0	3
Resistant phenotype	MRSA/MRS (cefoxitin)	SAU	N/A	99.5	184	141	43	86	N/A	98	0	1	N/A
		SLU	N/A	100	28	1	27	28	N/A	0	0	0	N/A
		CoNS	N/A	96.8	186	115	71	38	N/A	148	5	1	N/A
	MLSb (erythromycin-clindamycin)	SLU	N/A	100	29	1	28	27	N/A	2	0	0	N/A
		CoNS	N/A	97.8	135	135	0	67	N/A	68	1	2	N/A
		All	97.6	97.9	4142	2132	2010	3311	22	809	8	22	55

TABLE 6 Gram-negative AST results by organism/antimicrobial combination

Class	Antimicrobial	Organism[a]	EA (%)	CA (%)	No. of samples: Test	Fresh	Seed	No. of samples with the following AST result: S	I	R	No. of errors: VME	ME	mE
Aminoglycoside	Amikacin	Enteric	95.6	95.0	343	167	176	321	17	5	0	0	17
		PAE	97.6	100	42	12	30	31	0	11	0	0	0
		ABA	80.9	80.9	47	3	44	12	2	33	0	0	9
	Gentamicin	Enteric	99.7	99.7	343	177	166	293	3	47	0	0	1
		PAE	95.2	88.1	42	12	30	30	4	8	0	1	4
	Tobramycin	Enteric	96.0	96.0	347	179	168	284	11	52	0	0	14
		PAE	100	97.6	42	12	30	30	1	11	0	0	1
Carbapenems	Ertapenem	Enteric	98.9	98.6	351	181	170	316	6	29	0	2[c]	3
	Meropenem	Enteric	97.8	98.1	364	180	184	329	0	35	0	4[d]	3
		PAE	90.2	90.2	51	12	39	26	0	25	0	1	4
		ABA[b]	96.8	96.8	156	3	153	60	3	93	0	2	3
Cephalosporin	Cefazolin	Enteric[b]	95.3	85.8	274	144	130	131	27	116	0	0	39
	Cefepime	Enteric	97.7	96.9	349	180	169	280	6	63	1	0	10
		PAE	92.9	92.9	42	12	30	23	0	19	0	3	0
		ABA[b]	87.1	83.9	155	3	152	47	22	86	0	0	25
	Ceftazidime	Enteric	93.9	93.9	377	175	202	266	3	108	0	0	23
		PAE	90.6	88.7	53	12	41	25	0	28	0	6	0
	Ceftriaxone	Enteric	95.1[e]	96.6	324	166	158	215	2	107	0	0	11
Fluoroquinolone	Ciprofloxacin	Enteric	98.9	98.3	352	181	171	262	3	87	0	0	6
		PAE	92.9	97.6	42	12	30	28	0	14	0	0	1
		ABA[b]	96.8	98.1	155	3	152	51	1	103	0	0	3
Monobactam	Aztreonam	Enteric	96.6	97.7	348	179	169	257	3	88	1	1	6
Penicillin inhibitor	Ampicillin-Sulbactam	Enteric	92.2	84.2[g]	322	155	167	165	36	121	1	1	49
		ABA[b]	93.6	84.1	157	3	154	65	19	73	0	2	23
	Piperacillin-Tazobactam	Enteric	92.5	93.0	402	174	228	304	18	80	1	3[f]	24
		PAE	90.0	82.9	70	12	58	35	4	31	0	1	11
		ABA	97.9	97.9	47	3	44	5	0	42	0	1	0
Polymyxin	Colistin[b]	Enteric	93.3	97.9	329	152	177	314	0	15	3	4	0
		PAE	100	100	42	12	30	42	0	0	0	0	0
		ABA	90.4	91.9	136	3	133	132	0	4	1	10	0
Tetracycline	Minocycline[b]	ABA	97.4	92.1	227	3	224	198	12	17	0	1	17
All	All	All	95.4	94.3	6,331	2,522	3,809	4,577	203	1,551	8	43	307

Pancholi, P., et al. (2018). Multicenter Evaluation of the Accelerate PhenoTest BC Kit for Rapid Identification and Phenotypic Antimicrobial Susceptibility Testing Using Morphokinetic Cellular Analysis. Journal of clinical microbiology, 56(4), e01329-17.

Antibiogramas rápidos en hemocultivo positivo: Accelerate Pheno System

ACCELERATE DIAGNOSTICS

- Rapidez
- Buena concordancia con técnica de referencia
- Aprobación FDA

- Microorganismos diana limitados
- No útil en bacteriemias mixtas
- Precio
- Tamaño de cartucho
- Difícil de escalar a un alto número de muestras

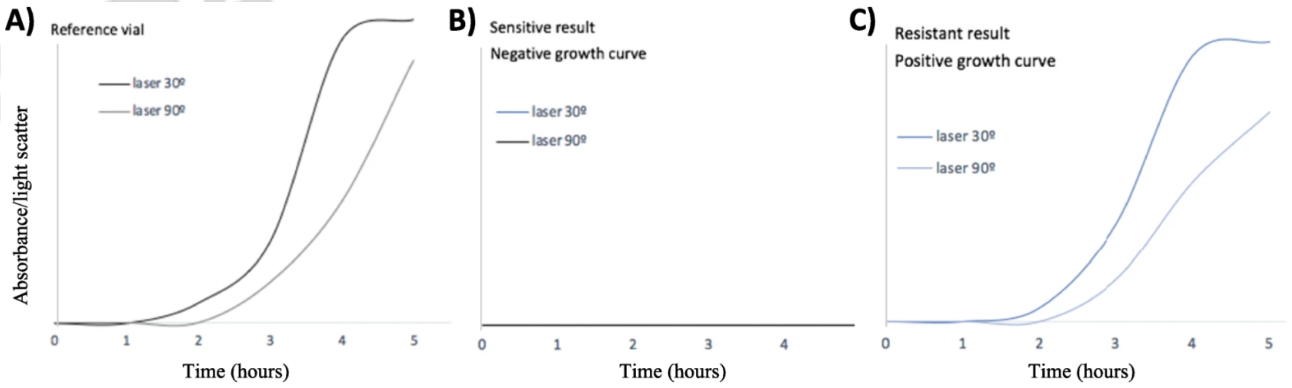
Antibiogramas rápidos en hemocultivo positivo: Alfred (AliFAX)

1 - Open view

2 - Primary samples

3 - Incubation and reading unit

4 - Refrigerated area for antibiotics and 0.5 McFarland bacterial suspension



Antibiogramas rápidos en hemocultivo positivo: Alfred (AliFAX)

Table 1 AST results of the Alfred 60AST™ system compared to BD Phoenix™ system for each antibiotic. Column 2 shows the total number of susceptibility tests done with both methods; columns 3 to 6 the total number of tests for which there was agreement within each category and in total; columns 8 to 10 the number of discrepancies; S = susceptible = intermediate, R = resistant, CA = Categorical agreement, 95% CI = 95% confidence interval

		No. of category agreements					No. of discrepancies		
Antimicrobial agent	No. of AST results	S	R	I	CA Total	CA % (95% CI)	Minor	Major	Very major
Gram-negative antimicrobials									
Ampicillin	301	88	202	0	290	96 (94–98)	0	4	7
Amikacin	298	273	2	2	277	93 (89–96)	3	17	1
Ciprofloxacin	297	222	61	0	283	95 (92–97)	1	7	6
Ceftriaxone	78	64	11	0	75	96 (89–99)	0	1	2
Gentamicin	297	240	38	1	279	94 (91–96)	1	10	7
Piperacillin/Tazobactam	295	263	16	1	280	95 (92–97)	0	10	5
Meropenem	297	284	4	0	288	97 (94–99)	0	6	3
Overall agreement	1863	1434	334	4	1772	95 (94–96)	5 (0.3%)	55 (3%)	31 (2%)
Gram-positive antimicrobials									
Cefoxitin	75	34	35	0	69	92 (83–97)	0	4	2
Cindamycin	75	41	17	2	60	80 (69–88)	1	9	5
Teicoplanin	86	79	0	1	79	92 (84–97)	1	6	0
Vancomycin	86	76	1	0	77	90 (81–95)	0	9	0
Ampicillin	11	9	1	0	10	90 (59–100)	0	1	0
Overall agreement	333	239	54	3	295	89 (85–92)	2 (0.6%)	29 (9%)	7 (2%)

Anton-Vazquez, V., Adjepong, S., Suarez, C., & Planche, T. (2019). Evaluation of a new Rapid Antimicrobial Susceptibility system for Gram-negative and Gram-positive bloodstream infections: speed and accuracy of Alfred 60AST. *BMC microbiology*, *19*(1), 268.

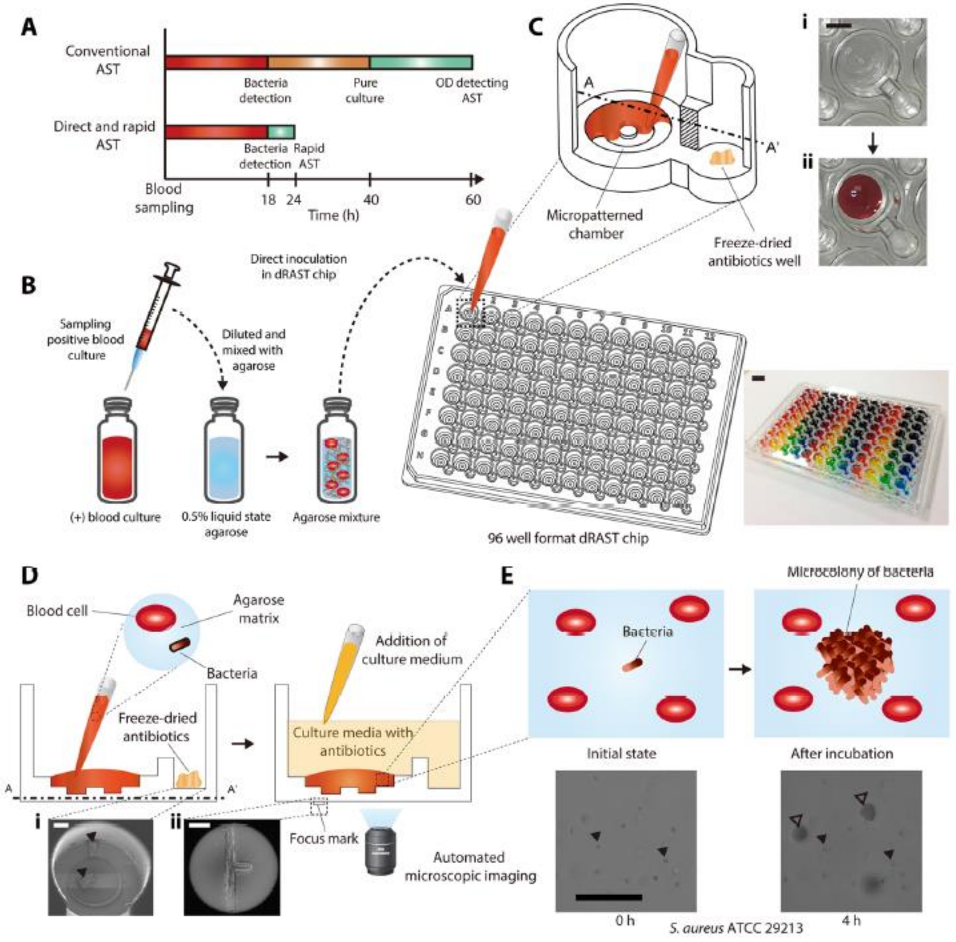
Antibiogramas rápidos en hemocultivo positivo: Alfred (AliFAX)

- Rapidez
- Buena concordancia con técnica de referencia
- Procesa varias muestras al mismo tiempo
- Panel de antibióticos que se utiliza es personalizable

- No realiza identificación bacteriana
- No útil en bacteriemias mixtas
- Precio (más reducido que otros métodos de la competencia)

Antibiogramas rápidos en hemocultivo positivo: QMAC-dRAST (QuantaMatrix)

QuantaMatrix



Nuevos sistemas automatizados de AST en el mercado: QMAC-dRAST (QuantaMatrix)

Table 2. Performance characteristics of the QMAC-dRAST by antibiotic and bacterial group.

	N° of Antibiotics Tested	CA	CA%	me	me%	ME	ME%S	VME	VME%R	S	S_%	R	R_%
Enterobacterales													
Amikacin	130	130	100							130	100	0	0.0
Amoxicillin–Clavulanate	130	125	96.2			3	5.9	2	2.5	51	39.2	79	60.8
Ampicillin	130	130	100							16	12.3	114	87.7
Ceftazidime	130	114	87.7	11	8.5	5	5.1			98	75.4	32	24.6
Ceftazidime–Avibactam	129	129	100							129	100	0	0.0
Ciprofloxacin	129	123	95.3	5	3.9	1	1			104	80.6	25	19.4
Cefepime	130	116	89.2	9	6.9	5	4.6			108	83.1	22	16.9
Gentamicin	130	125	96.2	4	3.1			1	5.6	112	86.2	18	13.8
Imipenem	118	103	87.3	15	12.7					115	97.5	3	2.5
Levofloxacin	130	120	92.3	10	7.7					114	87.7	16	12.3
Meropenem	130	129	99.2			1	0.8			129	99.2	1	0.8
Piperacillin–Tazobactam	130	122	93.8	6	4.6	1	1	1	3.4	101	77.7	29	22.3
Trimethoprim–Sulfamethoxazole	130	128	98.5	1	0.8	1	1.1			89	68.5	41	31.5
Non-fermentative GNB													
Amikacin	19	18	94.7	1	5.3					16	84.2	3	15.8
Ceftazidime	13	13	100							8	61.5	5	38.5
Ceftazidime–Avibactam	12	12	100							9	75	3	25.0
Ciprofloxacin	19	17	89.5	2	10.5					14	73.7	5	26.3
Cefepime	13	11	84.6			2	22.2			9	69.2	4	30.8
Gentamicin	18	18	100							12	66.7	6	33.3
Imipenem	19	18	94.7	1	5.3					12	63.2	7	36.8
Levofloxacin	19	17	89.5					2	25	11	57.9	8	42.1
Meropenem	19	17	89.5	2	10.5					14	73.7	5	26.3
Piperacillin–Tazobactam	13	11	84.6			2	20			10	76.9	3	23.1
Trimethoprim–Sulfamethoxazole	7	4	57.1	2	28.6	1	16.7			6	85.7	1	14.3
***Staphylococcus* spp.**													
Clindamycin	69	67	97.1	1	1.4	1	1.8			58	84.1	11	15.9
Daptomycin	69	68	98.6			1	1.4			69	100	0	0.0
Gentamicin	69	67	97.1			1	2	1	5.6	51	73.9	18	26.1
Linezolid	69	69	100							69	100	0	0.0
Levofloxacin	69	60	87	1	1.4	8	17			48	69.6	21	30.4
Oxacillin	69	46	66.7			16	50	7	18.9	32	46.4	37	53.6
Penicillin G	24	24	100							1	4.2	23	95.8
Teicoplanin	69	68	98.6			1	1.5			65	94.2	4	5.8
Vancomycin	69	69	100							69	100	0	0.0
***Enterococcus* spp.**													
Ampicillin	31	26	83.9	3	9.7	2	8			25	80.6	6	19.4
Gentamicin-Syn	31	30	96.8			1	3.7			27	87.1	4	12.9
Linezolid	31	30	96.8					1	100	30	96.8	1	3.2
Levofloxacin	26	24	92.3			2	11.1			18	69.2	8	30.8
Teicoplanin	31	31	100							24	77.4	7	22.6
Vancomycin	31	30	96.8			1	4.8			21	67.7	10	32.3
Total	2604	2459	94.4	74	2.8	56	2.8	15	2.6	2025	77.77	579	22.2

Rosselin, M., et al. (2022). Performance Evaluation of the Quantamatrix QMAC-dRAST System for Rapid Antibiotic Susceptibility Testing Directly from Blood Cultures. Microorganisms, 10(6), 1212.

Nuevos sistemas automatizados de AST en el mercado: QMAC-dRAST (QuantaMatrix)

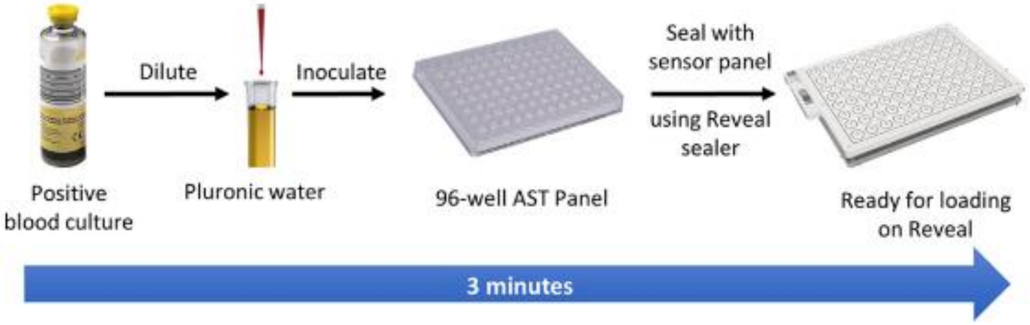
QuantaMatrix

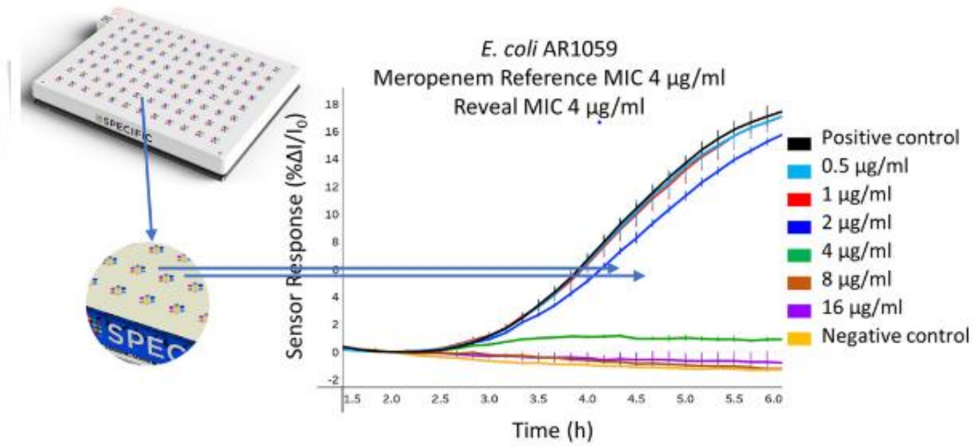
- Rapidez
- Buena concordancia con técnica de referencia (cuidado con algunos antibióticos)

- No realiza identificación bacteriana
- Precio
- Problemas de crecimiento bacteriano
- No aplicable en bacteriemias mixtas
- Difícil de escalar a un alto número de muestras
- Pocos datos de evaluación del mismo

Antibiogramas rápidos en hemocultivo positivo: Reveal (SPECIFIC)

SPECIFIC BIOMÉRIEUX





Antibiogramas rápidos en hemocultivo positivo: Reveal (SPECIFIC)

TABLE 2 Performance of the Reveal AST system for each species across all antimicrobials

Species and reference	Reveal avg TTR (h)	No. of strains[a]	No. of antibiotics[b]	No. of strains: Total[c]	S	I	R	% Agreement (no./total no.): EA	CA	No. of errors: mE	ME	VME
Sensititre as reference												
C. koseri	4.1	1	22	22	22	0	0	100 (22/22)	100 (22/22)	0	0	
E. cloacae	4.5	3	19	57	49	2	6	98.2 (56/57)	94.7 (54/57)	2	0	1
E. coli[d]	4.5	66	24	1,584	1,300	43	241	98.2 (1,491/1518)	96.2 (1,524/1584)	56	3	1
K. aerogenes	4.4	2	19	38	30	2	6	97.4 (37/38)	94.7 (36/38)	1	0	1
K. oxytoca[d]	4.8	3	23	69	69	0	0	95.5 (63/66)	95.7 (66/69)	3	0	
K. pneumoniae[d]	4.6	16	23	368	302	6	60	98.3 (346/352)	96.7 (356/368)	10	1	1
P. aeruginosa	4.6	10	12	120	117	3	0	95.0 (114/120)	94.2 (113/120)	6	1	
Overall		101		2,258	1,889	56	313	98.0 (2,129/2,173)	96.3 (2,174/2,258)	78	5	4
Vitek 2 as reference												
C. koseri	4.1	1	14	14	14	0	0	100 (14/14)	100 (14/14)	0	0	
E. cloacae	4.5	3	13	39	33	3	3	97.4 (38/39)	89.7 (35/39)	3	0	1
E. coli[d]	4.5	67	17	1,139	935	19	185	97.6 (1,046/1,072)	97.3 (1,108/1,139)	26	3	2
K. aerogenes	4.4	2	13	26	20	2	4	92.3 (24/26)	84.6 (22/26)	4	0	0
K. oxytoca[d]	4.8	3	16	48	47	1	0	93.3 (42/45)	93.8 (45/48)	3	0	
K. pneumoniae[d]	4.6	17	16	272	218	14	40	95.7 (244/255)	93.8 (255/272)	16	1	0
P. aeruginosa	4.6	11	7	77	75	2	0	96.1 (74/77)	97.4 (75/77)	2	0	
Overall		104		1615	1342	41	232	97.0 (1,482/1,528)	96.2 (1,554/1,615)	54	4	3

Tibbetts, R., George, S., Burwell, R., Rajeev, L., Rhodes, P. A., Singh, P., & Samuel, L. (2022). Performance of the Reveal Rapid Antibiotic Susceptibility Testing System on Gram-Negative Blood Cultures at a Large Urban Hospital. Journal of clinical microbiology, 60(6), e0009822.

Antibiogramas rápidos en hemocultivo positivo: Reveal (SPECIFIC)

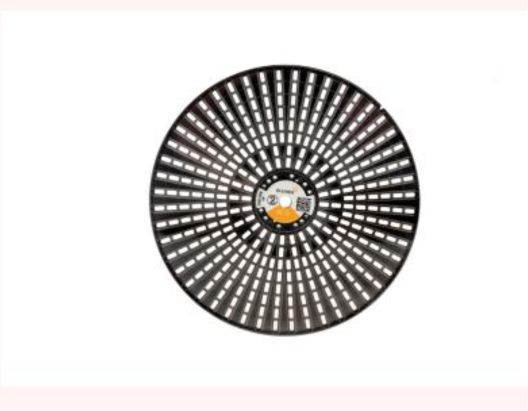
SPECIFIC

BIOMÉRIEUX

- Rapidez
- Buena concordancia con técnica de referencia

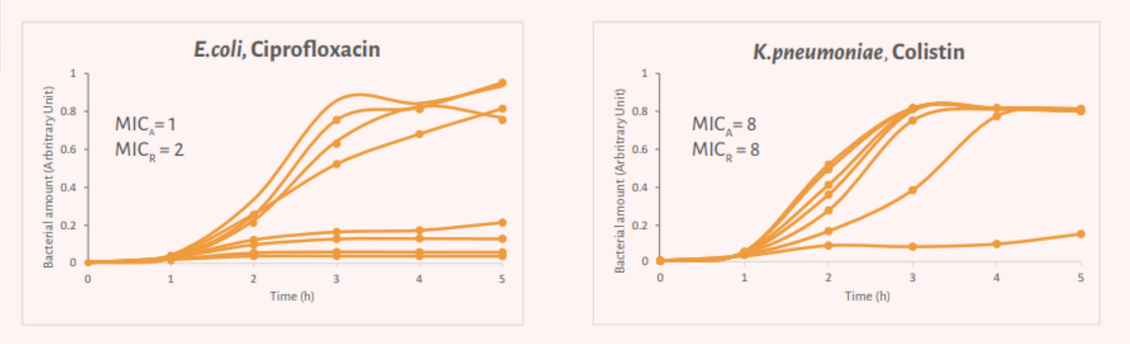
- No realiza identificación bacteriana
- No útil en bacteriemias mixtas
- Precio
- Difícil de escalar a un alto número de muestras

Antibiogramas rápidos en hemocultivo positivo: ASTar (Q-linea)



Q-LINEA

ThermoFisher
SCIENTIFIC



Antibiogramas rápidos en hemocultivo positivo: ASTar (Q-linea)

Timely Targeted Treatments in Sepsis.

ThermoFisher SCIENTIFIC

An evaluation of the real-time benefits of the Q-linea ASTar System on patient outcome by providing rapid direct blood culture sensitivities in Gram-negative organisms.

Results

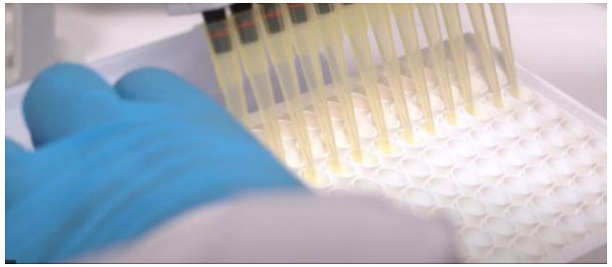
- Whiston STHK compared this novel rAST platform, including time to result (TTR), equivalence to in-house Vitek2 AST method and the gold-standard equivalent broth microdilution based Sensititre System.
- TTR was reduced from 28 hours (SOC) to 14 hours (rAST). Average processing time per sample was recorded, and the average time recorded was 2 minutes.
- A total of 96.8% of MIC values delivered by the ASTar System were within 1 dilution step to results generated by a gold-standard equivalent methodology (Sensititre plates).
- Amoxicillin clavulanic acid over-reported resistance through the ASTar System when compared to both in-house and gold-standard equivalent methodologies.

Total no. results		718
Total no. discrepancies		23
Essential agreement (%)		96.8
Discrepancy rates (%)		
Minor	Major	Very major
24.4	2.8	0.4

Whiston Hospital's scientific poster presentation from ECCMID 2022

Antibiogramas rápidos en hemocultivo positivo: Fastinov (Fastinov)

FASTinov
Next Generation
Antimicrobial Resistance Technologies



Antibiogramas rápidos en hemocultivo positivo: Fastinov (Fastinov)

GRAM NEGATIVOS

	EUCAST								CLSI							
	No. of strains by RM				No. (%) of errors				No. of strains by RM				No. (%) of errors			
BC type and antimicrobial agent	*n*	S	I	R	CA (%)	mE	ME	VME	*n*	S	I	R	CA (%)	mE	ME	VME
Spiked BC																
Ampicillin	130	26	NA	104	100				130	26		104	100			
Amoxicillin-clavulanic acid	130	35	NA	95	100				130	34	3	93	98.5	2/130 (1.5)		
Piperacillin-tazobactam	160	97	4	59	94.4	8/160 (5)	1/97 (1.0)		160	97	4	59	94.4	8/160 (5)	1/97 (1.0)	
Cefotaxime	130	50	3	77	95.4	5/130 (3.8)		1/77 (1.3)	130	50	3	77	95.4	5/130 (3.8)		1/77 (1.3)
Ceftazidime	160	63	2	95	95.0	8/160 (5)			160	65	7	88	94.4	7/160 (4.4)	1/63 (1.6)	1/88 (1.1)
Ceftolozane-tazobactam	160	111	NA	49	98.8		2/111 (1.8)		160	112		48	98.1	1/160 (0.6)	2/112 (1.8)	
Meropenem	192	119	6	67	95.3	7/192 (3.6)	2/119 (1.7)		192	112	5	75	97.9	4/192 (2.1)		
Imipenem	192	138	2	52	95.8	5/192 (2.6)	3/138 (2.2)		192	131	6	55	95.3	6/192 (3.1)	3/131 (2.3)	
Gentamicin	192	129	1	62	98.4	2/192 (1.0)	1/129 (0.8)		192	129	2	61	98.9	2/192(1.0)		
Amikacin	192	155	6	31	96.9	5/192 (2.6)	1/155 (0.64)		192	160	5	27	97.9	3/192 (1.6)	1/160 (0.63)	
Ciprofloxacin	192	92	4	96	94.8	8/192 (4.2)	2/92 (2.2)		192	96	5	91	94.8	8/192 (4.2)	2/92 (2.2)	
Colistin	192	172	NA	20	98.9		1/172 (0.6)		192	172	NA	20	98.9		1/172 (0.58)	
Total	2022	1187	28	807	96.9	48/2022 (2.4)	13/1187 (1.09)	1/807 (0.12)	2022	1184	40	798	97.1	46/2022 (2.3)	11/1184 (0.93)	2/798 (0.25)
Patient BC																
Ampicillin	64	14	NA	50	100.0				64	14		50	98.4	1/64 (1.6)		
Amoxicillin-clavulanic acid	64	39	NA	25	92.2		2/39 (5.1)	3/25 (12)	64	41	11	12	81.3	12/64 (18.8)		
Piperacillin-tazobactam	64	61	1	2	96.9	2/64 (3.1)			64	61	1	2	96.9	2/64 (3.1)		
Cefotaxime	64	52		12	98.4	1/64 (1.6)			64	52		12	98.4	1/64 (1.6)		
Ceftazidime	64	51	1	12	90.6	5/64 (7.8)		1/12 (8.3)	64	52	4	8	90.6	5/64 (7.8)		1/8 (12.5)
Ceftolozane-tazobactam	64	61	NA	3	100				64	61		3	100			
Meropenem	64	63		1	96.9		2/63 (3.2)		64	62	1	1	95.3	2/64 (3.1)	1/62 (1.6)	
Imipenem	64	63		1	96.9		2/63 (3.2)		64	61	2	1	87.5	6/64 (9.4)	2/61 (3.3)	
Gentamicin	64	53		11	96.9		1/53 (1.9)	1/11 (9.0)	64	53		11	96.9	1/64 (1.6)		1/11 (9.1)
Amikacin	64	61	1	2	95.3	1/64	2/61		64	62		2	96.9	2/64 (3.1)		
Ciprofloxacin	64	44		20	93.8	2/64 (3.1)	2/44 (4.5)		64	44		20	93.8	2/64 (3.1)	2/44 (4.5)	
Colistin	64	57	NA	7	100				64	57	NA	7	100			
Total	768	619	3	146	96.5	11/768 (1.4)	11/619 (1.8)	5/146 (3.4)	768	620	19	129	94.7	34/768 (4.4)	5/620 (0.80)	2/129 (1.6)
Overall FAST *gramneg* kit (spiked + patient BC)	2790	1808	24	958	96.8	59/2790 (2.1)	24/1808 (1.3)	6/958 (0.6)	2790	1805	58	927	96.4	80/2790 (2.9)	16/1805(0.9)	4/927 (0.4)

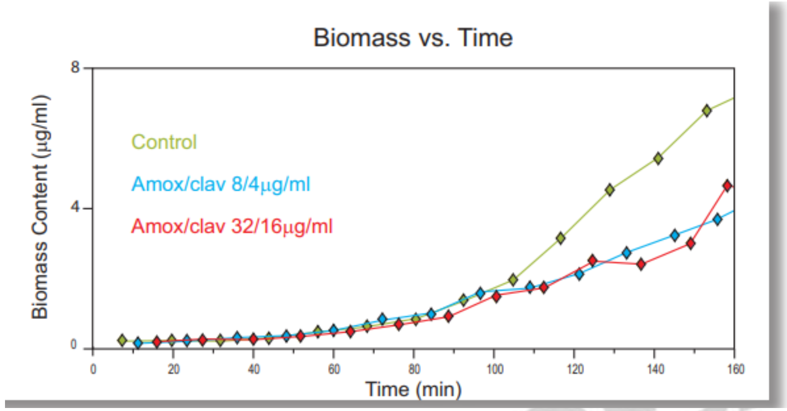
Silva-Dias A, Pérez-Viso B, Martins-Oliveira I, Gomes R, Rodrigues AG, Cantón R, Pina-Vaz C. Evaluation of FASTinov Ultrarapid Flow Cytometry Antimicrobial Susceptibility Testing Directly from Positive Blood Cultures. J Clin Microbiol. 2021 Sep 20;59(10):e0054421.

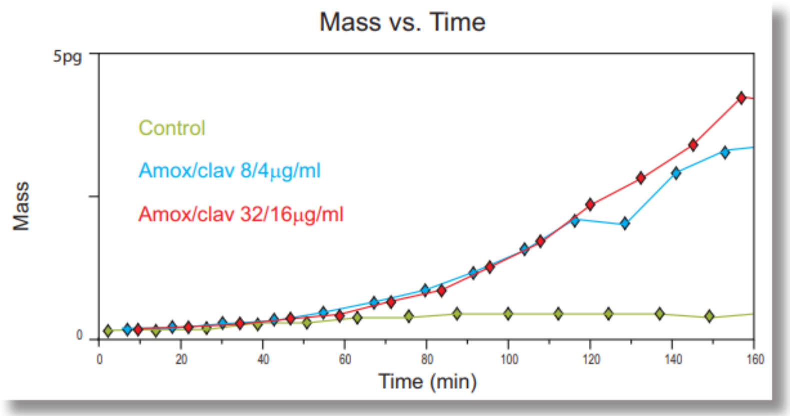
Antibiogramas rápidos en hemocultivo positivo: Fastinov (Fastinov)

GRAM POSITIVOS

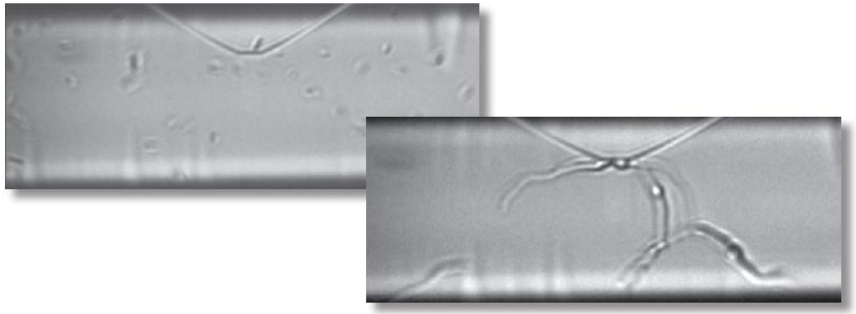
BC type and antimicrobial agent	EUCAST								CLSI							
	No. of strains by RM				No. (%) of errors				No. of strains by RM				No. (%) of errors			
	n	S	I	R	CA (%)	mE	ME	VME	*n*	S	I	R	CA (%)	mE	ME	VME
Spiked BC																
Linezolid	155	154	NA	1	100				155	154	NA	1	100			
Gentamicin	80	67	NA	13	98.8		1/67 (1.5)		80	68		12	98.8	1/80 (1.2)		
Gentamicin, high level	75	52	NA	23	100				75	56	NA	18	98.7		1/56 (1.8)	
Vancomycin	155	130	NA	25	98.0		3/130 (2.3)		155	130		25	98.0	2/155 (1.3)	1/130 (0.8)	
Cefoxitin	80	36	NA	44	98.8		1/36 (2.8)		80	36	NA	44	98.8		1/36 (2.8)	
Penicillin*	56	5	NA	51	98.2		1/5 (20)		155	48		107	98.1		3/49 (6.1)	
Ampicillin	75	44		31	97.3	1/75 (1.3)	1/44 (2.3)		75	44	NA	31	98.7		1/44 (2.3)	
Imipenem	75	38	1	36	96.0	2/75 (2.7)	1/38 (2.6)		NA	NA	NA	NA				
Total	751	526	1	224	98.5	3/751 (0.4)	8/526 (1.5)		775	536		238	98.7	3/775 (0.4)	7/536 (1.3)	
Patient BC																
Linezolid	36	36	NA		100				36	36	NA		100			
Gentamicin	36	23	NA	13	97.2			1/13 (7.7)	36	25		11	94.4	1/36 (2.7)	1/25 (4.0)	
Gentamicin, high level	0	0	NA	0					0	0	NA	0				
Vancomycin	36	36	NA		100				36	36			100			
Cefoxitin	36	17	NA	19	97.2		1/17(5.9)		36	17	NA	19	97.2		1/17(5.9)	
Penicillin*	10	2	NA	8	100				36	4		32	100			
Imipenem	0	0	0	0					0	0	0	0				
Total	154	114		40	98.7		1/114 (0.88)	1/40 (2.5)	180	118		62	98.1	1/118 (0.85)	2/62 (3.2)	
Overall FAST*grampos* kit (spiked + patient BC)	905	640	1	264	98.6	3/905 (0.3)	9/640 (1.4)	1/264 (0.4)	955	653		301	98.6	4/929 (0.4)	9/653 (1.4)	

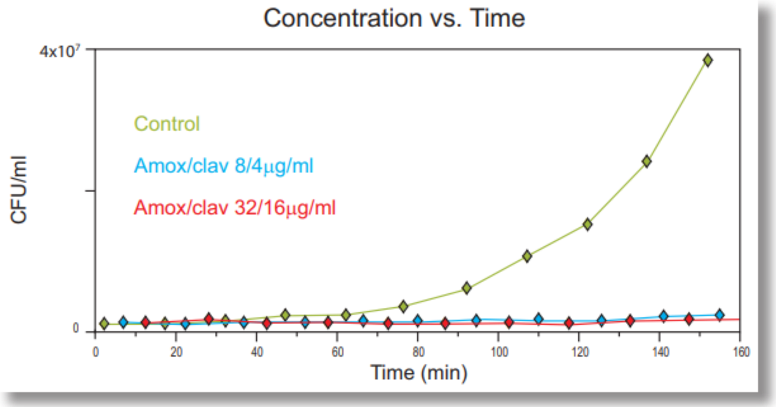
Antibiogramas rápidos en hemocultivo positivo: LifeScale (Affinity)





AFFINITY BIOSENSORS





Antibiogramas rápidos en hemocultivo positivo: LifeScale (Affinity)

Affinity Biosensors announces that University of Louisville Hospital completed its evaluation of the *LifeScale AST* rapid antibiotic susceptibility system and presented the results at IDWeek in Washington, DC

SANTA BARBARA, Calif., Nov. 8, 2022 /PRNewswire/ -- The study, titled *PERFORMANCE EVALUATION OF THE LIFESCALE AST RAPID AUTOMATED ANTIMICROBIAL SUSCEPTIBILITY SYSTEM*, assessed the performance of *LifeScale* compared to the Beckman Coulter *MicroScan WalkAway* AST System™. The study enrolled positive blood cultures from patient samples containing Gram-negative organisms. For the 1277 drug/bug combinations essential agreement was 96.50% and categorical agreement was 98.04%. There were no very major errors and only 3 major errors. Results were available in 4.5 hours and required ~8 minutes of hands-on time.

https://www.prnewswire.com/news-releases/university-of-louisville-hospital-presents-its-evaluation-of-the-affinity-biosensor-lifescale-rapid-ast-system-at-idweek-2022-301672120.html

¿Qué criterio seguir para realizar antibiogramas rápidos?

Quién

- ¿Paciente grave u oncohematológico?

Qué

- ¿Antibiograma por técnica rápida o por disco placa con lectura rápida?

Dónde

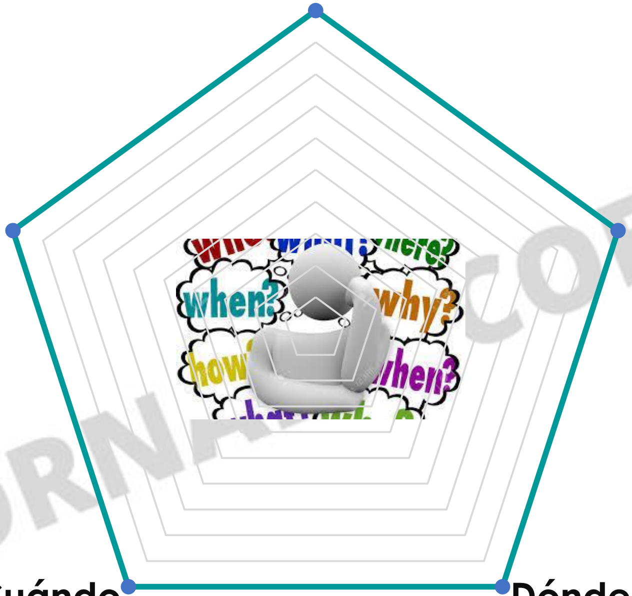
- ¿Hemocultivos u otras muestras relevantes?

Cuándo

- Lo antes posible ¿Hay atención continuada 24/7?

Por qué

- ¿El resultado va a condicionar la actitud terapéutica hacia al paciente?



GRACIAS

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