MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

Plan Nacional Resistencia Antibióticos

CoESAnt

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I Jornada del Comité Español del Antibiograma (COESANT)

Madrid 24 de noviembre de 2022

CoEsAnt

Documento CoEsAnt: antimicrobianos en paneles comerciales

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Documento CoEsAnt: antimicrobianos en paneles comerciales

Conflicts of interest

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

Clinical data coordinator (2007 – 2012, 2016 –)
Chairman (2012 – 2016)

CLSI

Member of the *Intrinsic Resistance Working Group* (2013 –)
Member of the Taxonomy group (2021 – 2022)
Advisor (2016 – 2017)

CoEsAnt

Member of *Comité Español del Antibiograma* (2014 – 2020)

Antimicrobial susceptibility testing

New approaches
for (*rapid*) AST

Automation
of AST

Interpretive reading
of the antibiograms

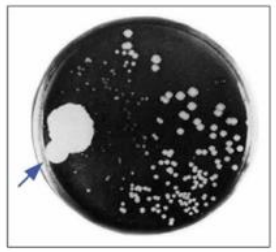
Interpretive
criteria (breakpoints)

Normalization of
in vitro AST

Relation between resistance
and clinical failure

Description of resistance
mechanisms and AST methods

Introduction of antibiotic
in therapeutics

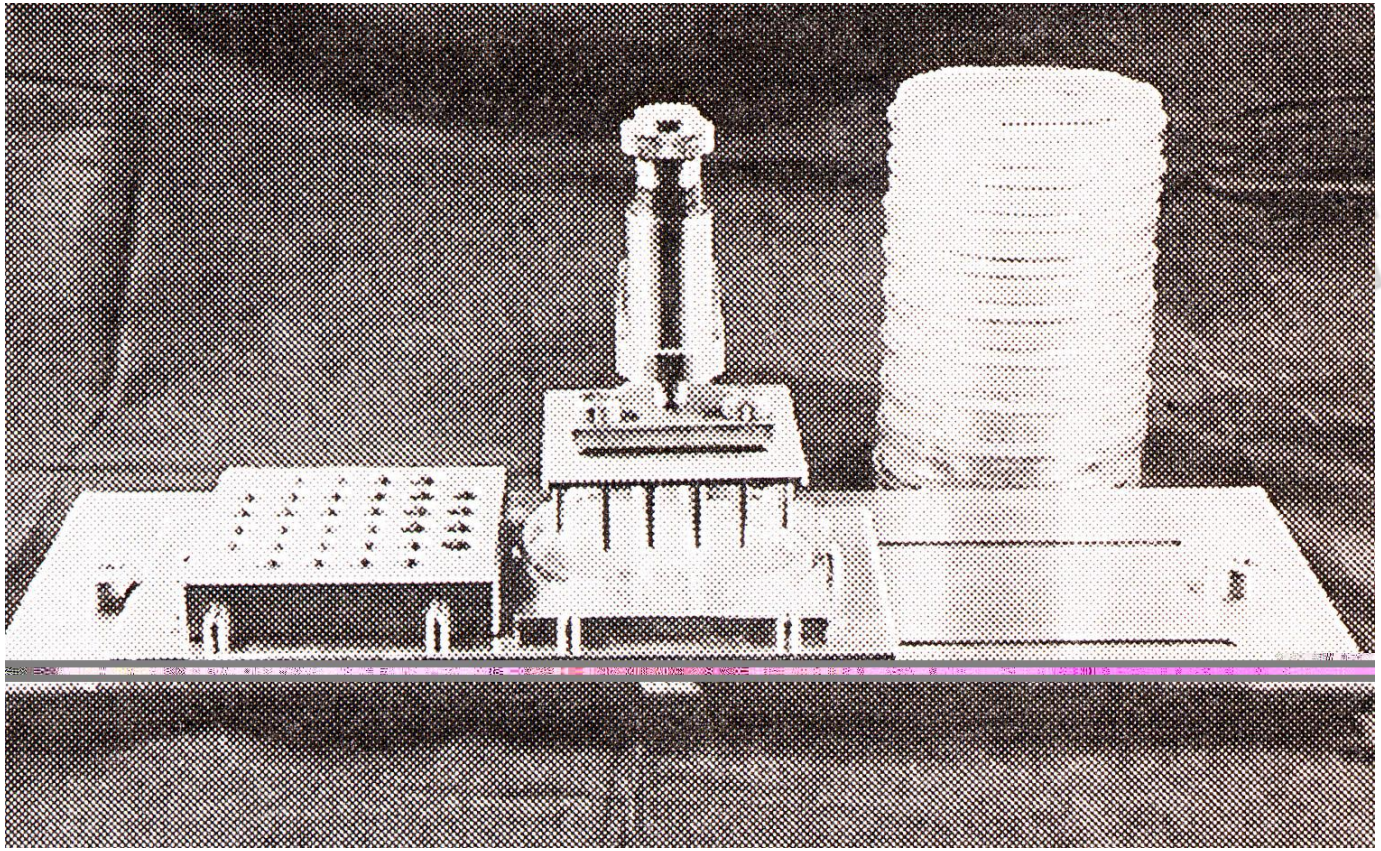


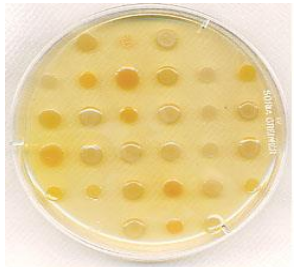
1920 1930 1940 1950 1960 1970 1980 1990 2000 2010 2020

Updated from Cantón R. Enf Inf Microbiol Clin 2002; 20:176-85

Antimicrobial susceptibility testing: automated/semi-automated systems

An early “automatic” device: **the Steers’s multi-inoculator (1959)** …





Steers E, Foltz F, Graves S, Riden J. An inocula replicating apparatus for routine testing of bacterial susceptibility to antibiotics. Antibiot Chemother 1959; 9:307-311

Antimicrobial susceptibility testing: automated/semi-automated systems

The first "automated short-incubation system": **The TAAS device (1971)**

(Technicon Instruments Corp. Tarrytown, NY, USA)

APPLIED MICROBIOLOGY, Dec. 1971, p. 980–986
Vol. 22, No. 6

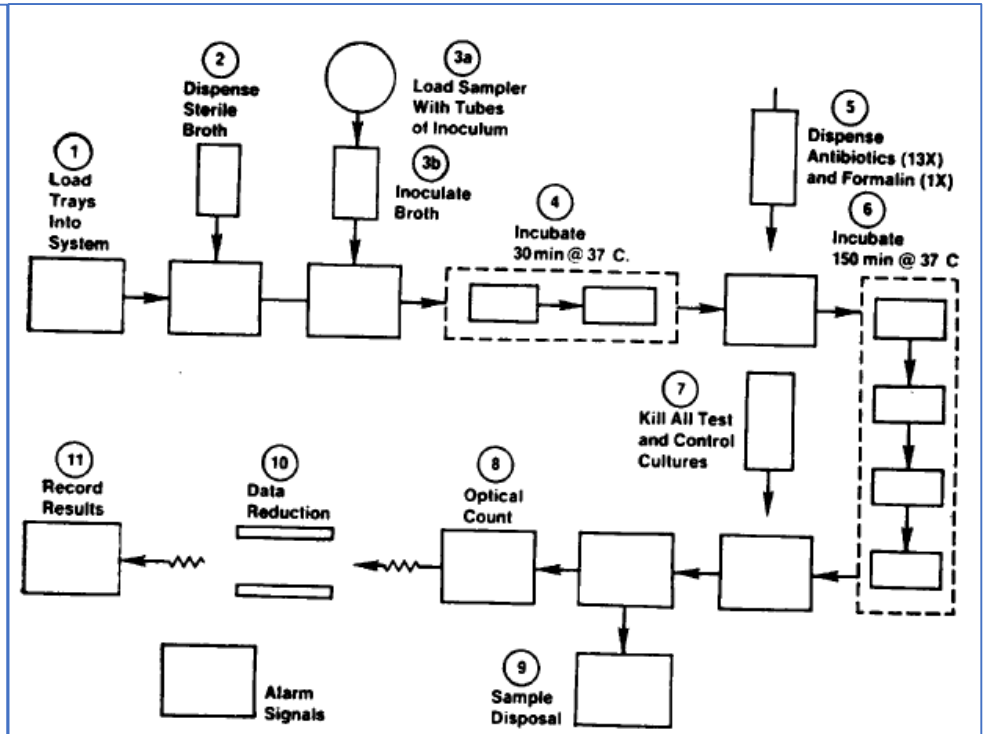
Prototype of a Fully Automated Device for Determination of Bacterial Antibiotic Susceptibility in the Clinical Laboratory[1]

HENRY D. ISENBERG, ALLEN REICHLER, AND DONALD WISEMAN

The Long Island Jewish Medical Center, New Hyde Park, New York 11040, and Technicon Instrument Corp., Tarrytown, New York 10591

Received for publication 12 July 1971

A completely automated system for the performance of antibiotic susceptibility tests in the clinical laboratory is described. With a modicum of personnel involvement, data on 40 specimens tested against 13 antibiotics are obtained every hour after an initial 3-hr period. The step by step explanation of the functioning of this prototype system, based on a thoroughly tested manual model, is presented. The system compares well with the standard diffusion test and has a potential for application to other endeavors of the clinical microbiology laboratory with a comparable saving in time and labor.



- Bacterial growth after 3-h incubation in the presence of one antimicrobial agent concentration was compared with a 3-h control with no drug

- The system includes:
  - inoculation unit
  - incubation unit
  - detection growth unit (optical recorder)

All these units are included in currently used automatic systems!

Antimicrobial susceptibility testing: automated/semi-automated systems

- None of the current **automated susceptibility testing devices** can be considered fully automated …

- Automated system consist of devices with computer-assisted incubation, reading, interpretation and reporting functions

- Semi-automated systems require off-line incubation*. The panels are automatically read with computer-assisted interpretation and reporting

*manual loading of each panel into the system is required

- Manual systems use commercial (eventually in-house) panels that are personnel. Results are either recorded by hand or manually entered into a computer for interpretation and reporting

- All instruments have implemented **informatics programs**

Antimicrobial susceptibility testing: automated/semi-automated systems

Classification

- MIC based systems
  - agar dilution (no longer exists!)
  - microdilution: MicroScan, Sensititre, Phoenix
  - growth curves: VITEK legacy, VITEK2
- Disc diffusion based systems
  - BIOMIC System
  - SIRSCAN System
  - OSIRIS System
  - Adagio system
  - ……

Antimicrobial susceptibility testing: automated/semi-automated systems

Automatic Systems for MIC determination

MicroScan
WalkAway 96 plus
Beckman

Vitek2 Compact
BioMèrieux

Phoenix M50 (x2)
DB

Sensititre ARIS HiQ
Thermo Fisher

Photos obtained from companies' brochures

Antimicrobial susceptibility testing: MIC based automatic systems

Device	Inoculation	Reading	Format	Combo (ID + AST)	Number of wells with antibiotics	Reporting time (h)		
						ID	AST	Resistance mechanism
Sensititre	Manual or semiautomatic	Manual read or Fluorescence	96 well panel	No Range of antb tested: ?	?	-	18-24	?
MicroScan	Manual or semiautomatic	Manual read or turbidity/colorimetry (Fluorometer)	96 well panel	Yes Range of antb tested: 25-34	BGN: 28 ID/65AST 93 AST CP: 26 ID/70 AST 93 AST	16-18 (2.5)	16-18 (6-12)	16-18 (6-12)
BD Phoenix M50	Manual or Semiautomatic	Redox and turbidity	136 well panel	Yes Range of antb tested: 20-34	51 ID/85 AST	3	4-16	4-8 CPO ≈ 7h
Vitek2	Semiautomatic	Fluorometer, photometer	64 well card	Yes (separate ID and antb cards) Range of antb tested: 14-32	BGN: 63 ID/113 AST (standard+extended) CP: 63 ID/60 AST	4	4-18	4-8

All these system fulfill FDA and ISO accuracy performance

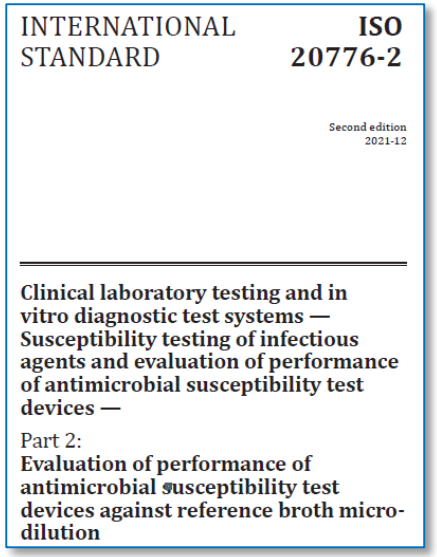
Updated information from Evangelista & Truant. In: Commercial methods in Clinical Microbiology. 2002
obtained with manufacturers brochures, key opinion/thought leaders and users

Antimicrobial susceptibility testing: automated/semi-automated systems

Acceptable performance for automated/semiautomated AST devices

Criteria	FDA (2009)	ISO 20776-2 (2007)	ISO 20776-2 (2021)
Essential agreement (± 1 dilution)	>89.9%	≥90.0%	≥90.0%
Category agreement (S / I / R)	>89.9%	≥90.0%	--
Major discrepancies (false resistance)	≤3%*	≤3%*	--
Very major discrepancies (false susceptibility)	≤1.5%**	≤1.5%**	--
Bias	--	--	+/- 30%
Growth failure rates:	< 10%***	--	--
Reproducibility	--	≥95.0%	≥95.0%

*based on the no. of susceptible organisms tested; **based on the no. of resistant organisms tested; ***for any genus or species tested


INTERNATIONAL STANDARD ISO 20776-2

Second edition 2021-12

Clinical laboratory testing and in vitro diagnostic test systems — Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices —

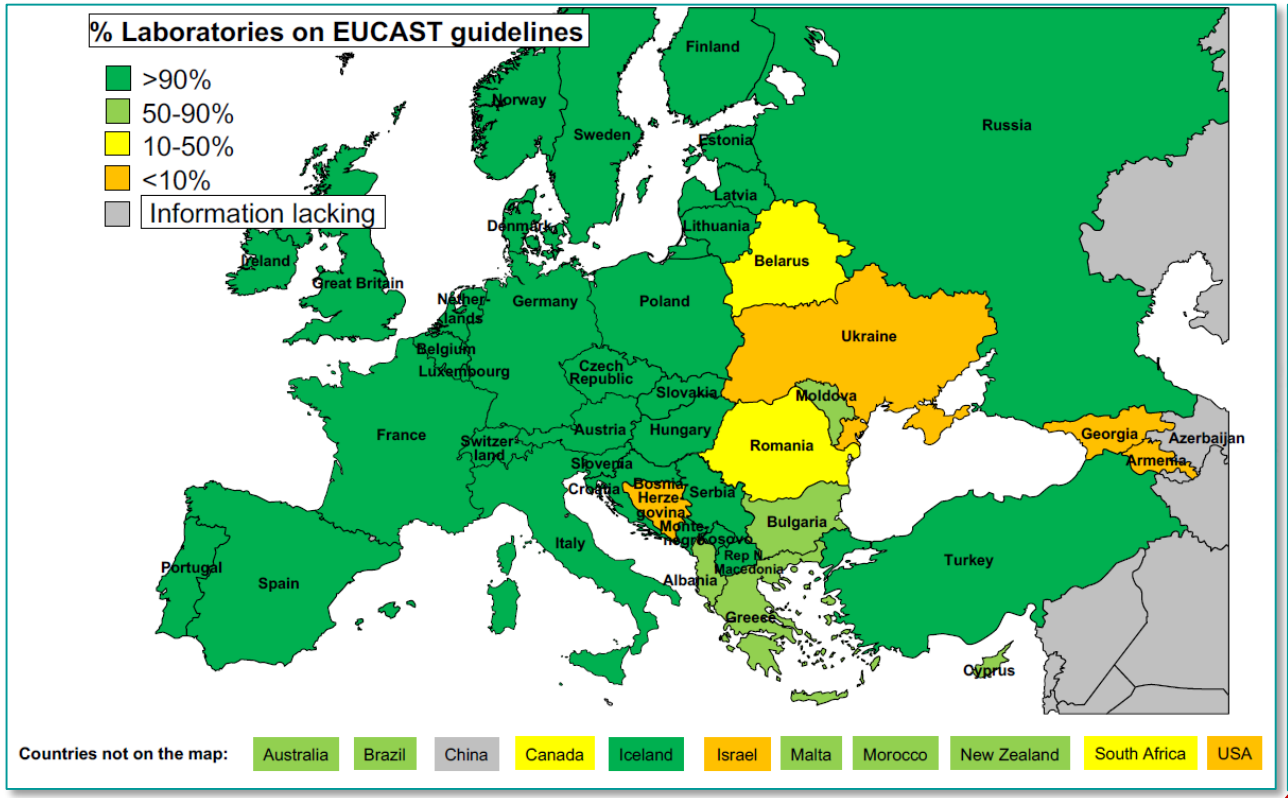
Part 2: Evaluation of performance of antimicrobial susceptibility test devices against reference broth micro-dilution

Antimicrobial Susceptibility Test (AST) Systems. Guidance for Industry and FDA. Class II Special Controls Guidance Document:, Aug 28, 2009. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080564.htm

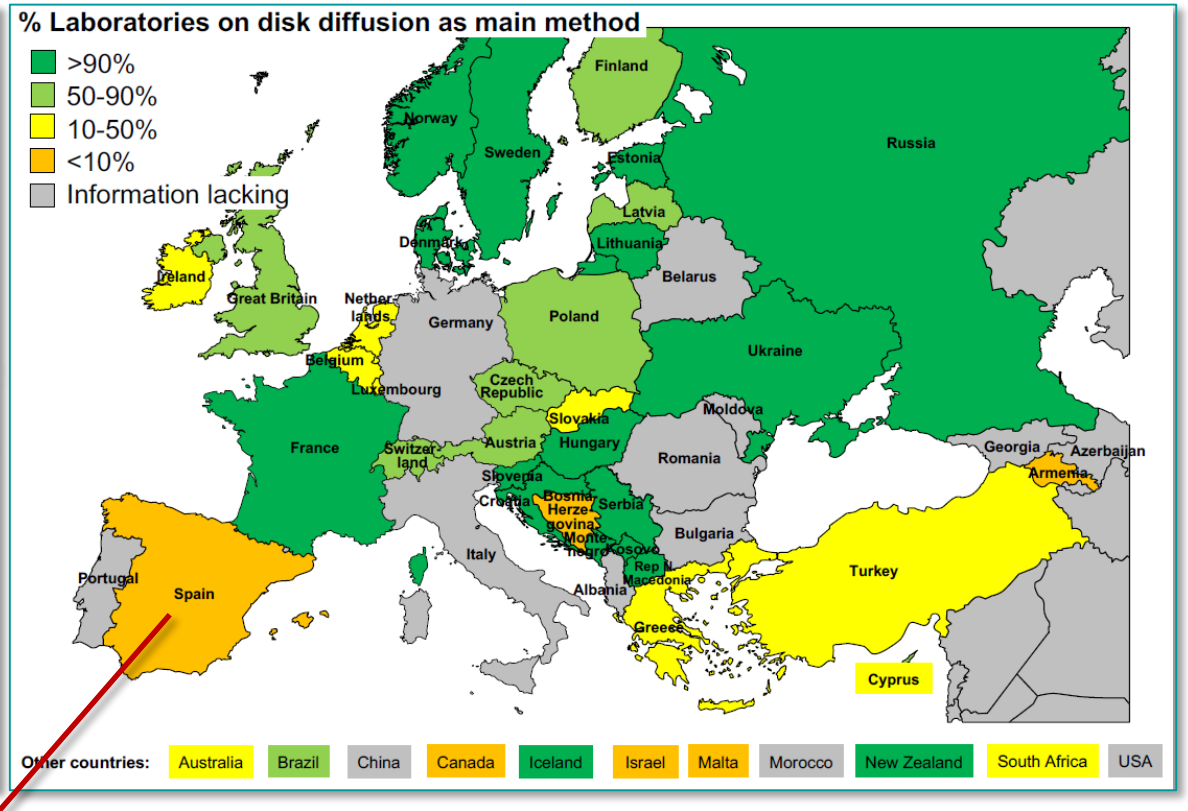
Clinical laboratory testing and in vitro diagnostic test systems - Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices - Part 2: Evaluation of performance of antimicrobial susceptibility test devices. International Standard ISO 20776-2:2007, ISO, Geneva. Updated 2021.

Implementation of EUCAST breakpoints, *March 2022*

Implementation of EUCAST in EU and beyond, March 2022



Use of EUCAST disk diffusion as main method, March 2022

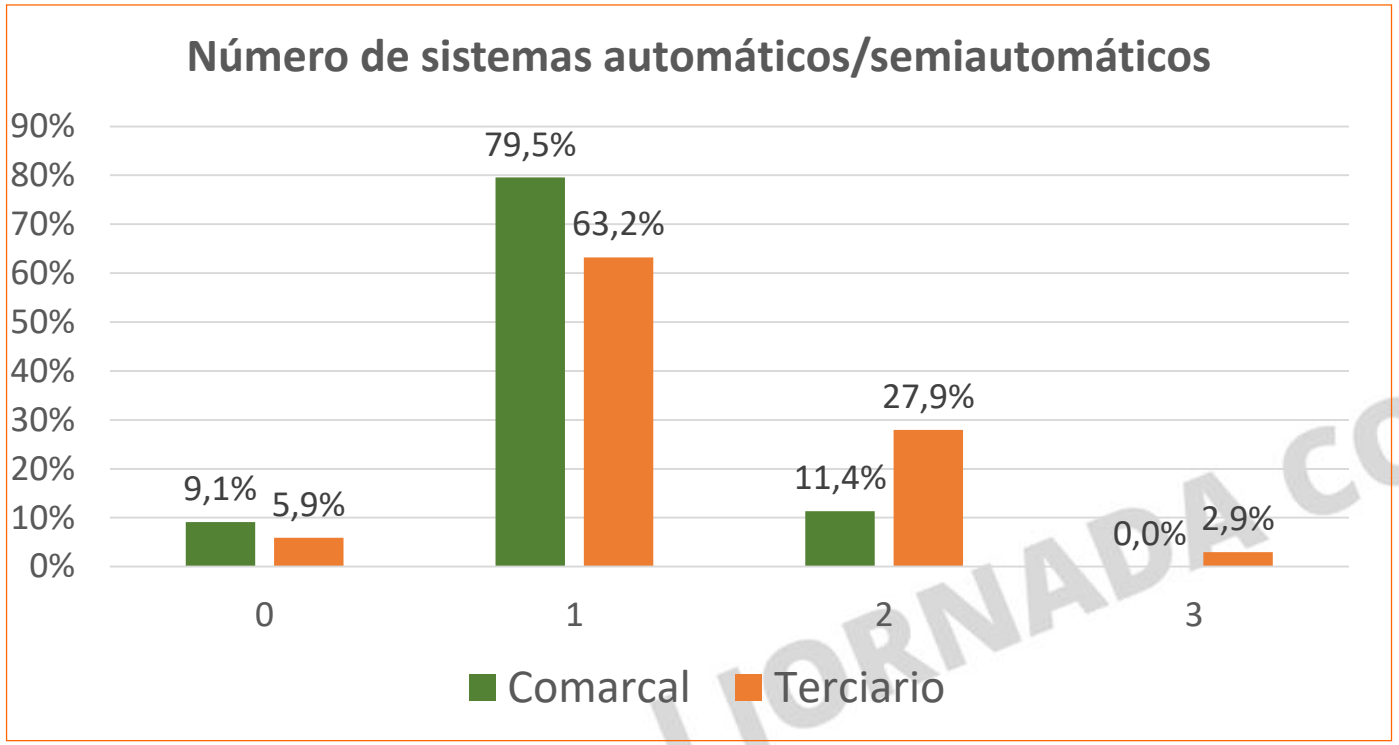


https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Statistics/EUCAST_Maps_March_2022.pdf

Extensive use of automated/semi-automated systems

Antimicrobial susceptibility testing in Spain

Sistema automáticos/semiautomáticos en el estudio de sensibilidad



Sistema	Total %
MicroScan	46,8%
Vitek	20,5%
Wider	1,3%
Phoenix	1,9%
MicroScan+Vitek	14,1%
MicroScan+Sensititre	2,6%
Vitek+Sensititre	0,6%
Phoenix+Wider	0,6%
Vitek+Wider	0,6%
MicroScan+Vitek+Wider	0,6%
MicroScan+Vitek+Sensititre	0,6%

Total de sistemas en España (n= 174)

Sistema	Nº	%
MicroScan	101	58,0%
Vitek	58	33,3%
Sensititre	6	3,4%
Wider	5	2,9%
Phoenix	4	2,3%

Encuesta Grupo de Estudio para la Gestión en Microbiología Clínica (GEGMIC) de la SEIMC. 2016

Antimicrobial susceptibility testing in Spain

Implementation of AST criteria throughout proficiency studies in Spain

Year	Microorganisms	CLSI	EUCAST	CLSI+EUCAST	Reference
2001	Enterobacterales, *Pseudomonas aeruginosa*	100%[2]	-	-	Cantón et al. JCM 2003; 41:1928-8
2007	*Escherichia coli* *Klebsiella penumonie*	98.2%	1.7%[1]	-	Conejo M et al. DMID 2008; 62:317-25
2013	*Pseudomonas aeruginosa*	86.1%	11.9%		Juan C et al. JAC 2013; 68:619-30
2012	Enterobacterales	67.2%	25.0%	1.6%	Ripoll et al. JCM 2014; 52:122-9
2014	*Acinetobacter* spp.	65%	19%	16%	Fdez -Cuenca et al. JAC 2018; 63:692-97
2015	Enterobacterales	53.3%	46.7%	-	Díez-Aguilar et al. IJAAC 2018; 51:612-9
2018	*Enterococcus* spp.	34.7%	65.3%	-	Fdez -Cuenca et al. EIMC (*in press*)
2018	*Staphylococcus aureus*	30.0%	70.0%	-	Fdez -Cuenca et al. JAC 2021; 76:1187-96

[1]MENSURA criteria; [2]15% simultaneously with MENSURA criteria

64.8% MicroScan; 28.4% Vitek2; 1.4% Phoenix; 2.1% MIC strips

Antimicrobial susceptibility testing: automated/semi-automated systems

Recomendaciones para la selección de antimicrobianos en el estudio de la sensibilidad *in vitro* con sistemas automáticos y semiautomáticos

Rafael Cantón[a], Juan Ignacio Alós[b], Fernando Baquero[a], Jorge Calvo[c], José Campos[d], Javier Castillo[e], Emilia Cercenado[f], M. Ángeles Domínguez[g], Josefina Liñares[g], Lorena López-Cerezo[h], Francesc Marco[i], Beatriz Mirelis[j], María-Isabel Morosini[a], Ferran Navarro[j], Antonio Oliver[k], Emilio Pérez-Trallero[l], Carmen Torres[m] y Luis Martínez-Martínez[c] en representación del Grupo de Consenso de Recomendaciones para la Selección de Antimicrobianos y Concentraciones en el Estudio de la Sensibilidad *in vitro* con Sistemas Automáticos y Semiautomáticos*

[a]Servicio de Microbiología. Hospital Universitario Ramón y Cajal. Madrid. [b]Servicio de Microbiología. Hospital Universitario de Getafe. Madrid. [c]Servicio de Microbiología. Hospital Universitario Marqués de Valdecilla. Santander. [d]Laboratorio de Antibióticos. Servicio de Bacteriología. Centro Nacional de Microbiología. Instituto de Salud Carlos III. Majadahonda. Madrid. [e]Servicio de Microbiología. Hospital Clínico Universitario. Zaragoza. [f]Servicio de Microbiología. Hospital Universitario Gregorio Marañón. Madrid. [g]Servicio de Microbiología. Hospital Universitario de Bellvitge. Hospitalet de Llobregat. Barcelona. [h]Servicio de Microbiología. Hospital Universitario Virgen Macarena. Sevilla. [i]Servicio de Microbiología. Hospital Clínic. Barcelona. [j]Servicio de Microbiología. Hospital de Sant Pau. Barcelona. [k]Servicio de Microbiología. Hospital Son Dureta. Palma de Mallorca. [l]Servicio de Microbiología. Hospital Donostia. San Sebastián. [m]Área de Bioquímica y Biología Molecular. Universidad de La Rioja. Logroño. España.
*Véase al final del artículo la relación de miembros del Grupo de Consenso de Recomendaciones para la Selección de Antimicrobianos y Concentraciones en el Estudio de la Sensibilidad *in vitro* con Sistemas Automáticos y Semiautomáticos designado por GEMARA y MENSURA

Enferm Infecc Microbiol Clin 2007;25(6):394-400

Objetivo

Establecer recomendaciones generales para la inclusión de antimicrobianos y la selección de sus concentraciones en los paneles y tarjetas de estudio de sensibilidad con sistemas automáticos y semiautomáticos en España

gemara
GRUPO DE ESTUDIO DE LOS MECANISMOS DE ACCIÓN Y DE LA RESISTENCIA A LOS ANTIMICROBIANOS

MENSURA

Mesa Española para la normalización de la susceptibilidad y resistencia a los antimicrobianos

BD · BIOMÉRIEUX · DADE BEHRING *Every minute of every day™* · FRANCISCO SORIA MELGUIZO, S.A. · IZASA

Antimicrobial susceptibility testing: automated/semi-automated systems

REVISIÓN — Enferm Infecc Microbiol Clin 2007;25(6):394-400

Recomendaciones para la selección de antimicrobianos en el estudio de la sensibilidad *in vitro* con sistemas automáticos y semiautomáticos

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Criterios		CATEGORÍAS (grado de recomendación según criterio de lectura interpretada)		
		A	B	C
GRUPOS (elección en el antibiograma según interés clínico para su información)	0	A0	B0	C0
	1	A1		
	2	A2	B2	
	3		B3	C3
	4	A4	B4	C4

Criterios de sección de antimicrobianos

- Antibióticos de interés clínico
- Antibióticos empleados en la vigilancia epidemiológica de la resistencia
- Antibióticos útiles en la lectura interpretada del antibiograma para la inferencia de posibles mecanismos de resistencia

Categoría A. Debe incluirse
Categoría B. Es recomendable su inclusión
Categoría C. Su inclusión es secundaria aunque facilita la lectura interpretada antibiograma

Criterios de selección de concentraciones

- Cubrir concentraciones críticas de antimicrobianos utilizadas para la definición de las categorías clínicas (S / I / R) definidas por los comités CLSI, EUCAST y MENSURA
- Concentraciones útiles para la vigilancia epidemiológica, cubrir rangos de distribuciones naturales o para facilitar la lectura interpretada del antibiograma

Antimicrobial susceptibility testing: automatic systems

REVISIÓN

Enferm Infecc Microbiol Clin 2007;25(6):394-400

Recomendaciones para la selección de antimicrobianos en el estudio de la sensibilidad *in vitro* con sistemas automáticos y semiautomáticos

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Criterios		CATEGORÍAS (grado de recomendación según criterio de lectura interpretada)		
		A	B	C
GRUPOS (elección en el antibiograma según interés clínico para su información)	0	A0	B0	C0
	1	A1		
	2	A2	B2	
	3		B3	C3
	4	A4	B4	C4

Criterios de inclusión de antimicrobianos

- **Categorías**
  - **Categoría A**. Debe incluirse
  - **Categoría B.** Es recomendable su inclusión
  - **Categoría C**. Su inclusión es secundaria aunque facilita la lectura interpretada antibiograma

- **Grupos de antimicrobianos**
  - **Grupo 0.** No utilizados en la clínica pero sirven para la detección de mecanismos de resistencia
  - **Grupo 1.** Se deben estudiar e informar por norma
  - **Grupo 2.** Se deben estudiar de manera habitual e informar selectivamente
  - **Grupo 3.** Se deben estudiar en un segundo nivel según el paciente, características de la infección, mecanismo de resistencia, etc., y se deben informar selectivamente
  - **Grupo 4.** Se deben estudiar siempre en los patógenos aislados de orina

Antimicrobial susceptibility testing: automated/semi-automated systems

Antibióticos y concentraciones para la determinación de la sensibilidad de *Haemophilus influenzae*

Antimicrobianos		Concentraciones (µg/ml)	Criterios
Betalactámicos	Amoxicilina	16-8-**4-2-1-0,5-0,25**	A1
	Amoxicilina/ácido clavulánico	8/4-**4/2-2/1-0,5/0,25-0,25/0,12**	A1
	Cefaclor	**32-16-8-4**-2	A2
	Cefuroxima	**16-8-4-2-1**-0,5-0,25	A2
	Cefotaxima	4-**2-1-0,5-0,25-0,12-0,06**	A2*
	Meropenem	4-**2-1-0,5-0,25-0,12-0,06**	A2*
Quinolonas	Ácido nalidíxico	**4**	C3**
	Ciprofloxacino	2-**1-0,5-0,25-0,12-0,06**	A1
MLS_B	Azitromicina	**4-2-1-0,5**-0,2	A1
	Telitromicina	**8-4-2**-1-0,5-0,2	C3
Tetraciclinas	Tetraci[illegible]	16-8-**4-2**-1	A2
		16-8-4-**2-1**	C3
		4-**2-1-0,5**-0,2	C3
Otros		**4-2-1**-0,5	A2*
		4/76-**2/38-1/19-0,5/9,5**	A2
		4-**2-1**-0,5	B3

Se decide su reedición revisión en la primera reunión de COESANT 7 de marzo de 2012

concentraciones que incluyen los puntos de corte (negrita)

Cantón R et al. Enferm Infecc Microbiol Clin 2007; 25:339-400

Antimicrobial susceptibility testing (AST): automatic systems

New scenario encouraging the update the 2007 document of AST with automatic systems

- **End of harmonization process** of clinical breakpoints in EU lead by EUCAST
  - introduction of **epidemiological cut-off values (ECOFF)** to recognize wild-type populations
  - **new definitions** of clinical breakpoints: susceptible, susceptible increased exposure, resistant
  - **area of technical uncertainty** (ATU)
- Foundation of **COESANT** (*Comité Español del Antibiograma*) aligned with EUCAST
- Introduction of **new antimicrobials** (β-lactam/β-lactamase inhibitor combinations, …) and **new indications**
- Description of **new resistance mechanisms**
  - new carbapenemases, plasmid mediated fluoroquinolone resistance, colistin resistance (*mcr*), linezolid resistance (*cfr, optrA,…*), methytransferases affecting aminoglycosides (ArmA/RmtA) …
- Implementation of **national plans** to address the problem of antimicrobial resistance
- Implementation of **antimicrobial stewardship programs**
- Introduction of **mass spectrometry identification** (MALDITOF MS)

Antimicrobial susceptibility testing: automated/semi-automated systems

Enferm Infecc Microbiol Clin. 2020;38(4):182–187

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Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Review article

Recommendations of the Spanish Antibiogram Committee (COESANT) for selecting antimicrobial agents and concentrations for *in vitro* susceptibility studies using automated systems

Rafael Cantón[a,b,*], Antonio Oliver[b,c], Juan Ignacio Alós[d], Natividad de Benito[e], Germán Bou[b,f], José Campos[b,g], Jorge Calvo[b,h], Andrés Canut[i], Javier Castillo[j], Emilia Cercenado[k], Maria Ángeles Domínguez[b,l], Felipe Fernández-Cuenca[b,m], Jesús Guinea[k], Nieves Larrosa[b,n], Josefina Liñares[b,a], Lorena López-Cerero[b,m], Antonio López-Navas[o], Francesc Marco[b,p], Beatriz Mirelis[q], Miguel Ángel Moreno-Romo[r], María Isabel Morosini[a,b], Ferran Navarro[q], Jesús Oteo[b,g], Álvaro Pascual[b,m], Emilio Pérez-Trallero[s], María Pérez-Vázquez[b,g], Alex Soriano[t], Carmen Torres[u], Jordi Vila[b,p], Luis Martínez-Martínez[b,w]

Objetives

- To **update** the general recommendations for the **selection of the antibiotics and their concentrations** to be included in the AST panels used by **automated/semiautomated systems** commercialized in Spain that was published in 2007
- To include **recommendations and criteria for selective reporting**
- To establish **criteria in the absence of those defined by EUCAST**
- To establish **minimum requirements** of automated/semi-automated systems

seimc Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica

gemara Grupo de Estudio de los Mecanismos de Acción y de la Resistencia a los Antimicrobianos

CoESAnt

Plan Nacional Resistencia Antibióticos

agencia española de medicamentos y productos sanitarios

Antimicrobial susceptibility testing: automated/semi-automated systems

Criteria for the selection of antimicrobials

Criteria	Reasons
Microbiological	Interpretive reading Inference of resistance mechanisms Epidemiology of resistance mechanisms (surveillance) Class representative compounds
Pharmacockinetic/ pharmacodynamic (PK/PD)	Selection of appropriate/ therapeutic options Representation for an antimicrobial class Inference of susceptibility to other antimicrobial
Clinical	

Cantón R et al. Enferm Infecc Microbiol Clin 2020; 38:182-7

Antimicrobial susceptibility testing: automatic systems

Criteria for the selection of antimicrobial concentrations

- **Mandatory** (bold)

  - Concentrations covering EUCAST clinical breakpoints (S / I / R) (**bold**)

Cefepime	0.125-**0.25-0.5-1-2-4-8**-16-32

ECOFF **S** **R**

- **Recommended** (not indicated in bold)

  - An additional concentration one dilution below the susceptible (S) breakpoint
  - Concentrations covering the ECOFF values to facilitate
    - detection of wild-type populations
    - epidemiological surveillance, especially of microorganisms with low-level resistance mechanisms
    - interpretive reading of the antibiogram

Cantón R et al. Enferm Infecc Microbiol Clin 2020; 38:182-7

Antimicrobial susceptibility testing: automated/semi-automated systems

Categories for the inclusion of the antimicrobials in AST panels for automated systems

(≈ *selective reporting*)

Category	Definitions
A	Antimicrobials that must be **routinely studied and reported** **-** relevant for both clinical purpose and for the process of interpretive reading of the antibiogram
B	Antimicrobials that must be **routinely studied but selectively reported** - useful for the process of interpretive reading - should be selectively reported according to the patient, infection or the inferred resistance mechanism
C	Antimicrobials that should be **selectively studied and reported** - according to the type of patient, type of infection or to the inferred resistance mechanism
D	Antimicrobials that are recommended to be **routinely studied and reported in urine** isolates
E	Antimicrobials that **should be studied but not reported**. - useful for the detection of resistance mechanisms - application of an expert rule - surrogate markers of the susceptibility testing result of other antimicrobials

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Antimicrobial susceptibility testing: automated/semi-automated systems

Antibiotics and concentrations recommended for the susceptibility testing (Tables)

- Enterobacterales
- *Pseudomonas* spp.
- *Acinetobacter* spp.
- *Stenotrophomonas maltophilia*
- Gram-(–) bacilli other than *Pseudomonas* spp., *Acinetobacter* spp. and *S. maltophilia*

- *Staphylococcus* spp.
- *Streptococcus pneumoniae* and other streptococci (including viridans streptococci and β-haemolytic groups A, B, C and G)
- *Enterococcus* spp.

- *Haemophilus* spp. (can be also applied for *H. parainfluenzae)*

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Antimicrobial susceptibility testing: automatic systems

Antibiotics and concentrations recommended for the susceptibility testing of Enterobacterales

Antimicrobial	Concentrations (mg/L)	Category	Comments
Ampicillin	2-**4**-**8**-**16**-32	A	Report as amoxicillin.
Amox-clav	**2/2-4/2-8/2-16/2-32/2**	A	The concentration of clavulanic ac. is fixed at 2 mg/L. ECOFF has not yet been defined. Breakpoints for uUTI has been defined as S ≤32/2 mg/L and R >32/2
Ticarcillin	4-**8**-**16**-**32**-64	E	It can be useful to infer the presence of resistance mechanisms, such as TEM-1, chromosomal AmpC hyperproduction or plasmid-mediated AmpC.
Piper-tazob	4/4-**8/4**-**16/4**-**32/4**-64/4	A	
Cefazolin	2-4-**8**-**16**-32	D	Used as a surrogate test for uUTI treated with oral cephalosporins. Breakpoints not defined by EUCAST; those shown are recommended by COESANT. ECOFF has not yet been defined
Cefuroxime	1-2-**4**-**8**-**16**-32	A	Breakpoints for iv and oral (uUTIs) formulations are the same. iv defined for *E. coli*, *K. pneumoniae* and *P. mirabilis* only. Oral breakpoints defined for uncomplicated UTI only
Cefoxitin	4-**8**-**16**-32	E	Breakpoints not defined by EUCAST. Cefoxitin MIC >8 mg/L may indicate high-level expression of AmpC β-lactamases (with the exception of ACC β-lactamases) or, in some organisms, porin deficiency

Bold: minimum no. of concentrations that are recommended to be included in the study of susceptibility testing; Underlined: ECOFF values (when lacking is due to the absence of definition by EUCAST). When different ECOFFs exist for the different enterobacterial species, the *E. coli* ECOFF is indicated; Light: I category; Dark gray: R category

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Antimicrobial susceptibility testing: automatic systems

Antibiotics and concentrations recommended for the susceptibility testing of Enterobacterales

Antimicrobial	Concentrations (mg/L)	Category	Comments
Ceftazidime	**0.5**-1-**2**-4-**8**-16-32	A	
Ceftazidime-clav	**1/4**-2/4-4/4-**8/4**	E	Recommended for confirmation of ESBL production in *E. coli*, *Klebsiella* spp., *P. mirabilis*, *Salmonella* spp., and *Shigella* spp.
Cefotaxime	**0.25**-0.5-1-**2**-4-**8**-16-32	A	
Cefotaxime-clav	**1/4**-2/4-4/4-**8/4**	E	Recommended for confirmation of ESBL production in *E. coli*, *Klebsiella* spp., *P. mirabilis*, *Salmonella* spp., and *Shigella* spp.
Cefixime	0.5-**1**-**2**-4-**8**-16	C	Breakpoints defined for uncomplicated UTI only. ECOFF has not yet been defined.
Cefepime	0.125-**0.25**-0.5-1-**2**-4-**8**-16-32	A	
Cefepime-clav	**1/4**-2/4-4/4-**8/4**	E	Recommended for confirmation of ESBL production in *Enterobacter* spp., *C. freundii* complex, *M. morganii*, *P. stuartii*, *Serratia* spp., and *H. alvei*. It is also useful for *E. coli* hyperproducing chromosomal AmpC or producing plasmidic AmpC.
Ceftolozane-tazob	0.5/4-**1/4**-**2/4**-**4/4**-8/4	C	ECOFF has not yet been defined. The concentration of tazobactam is fixed at 4 mg/L.
Cefta-avibactam	**0.5/4**-**1/4**-**2/4**-**4/4**-**8/4**-16/4	C	ECOFF has not yet been defined. Used to infer class A and D carbapenemases in isolates that are resistant to carbapenems. The concentration of avibactam is fixed at 4 mg/L.
Aztreonam	0.25-**0.5**-1-**2**-4-**8**-16-32	A	
Imipenem	0.25-**0.5**-1-**2**-4-**8**-16	A	>1 mg/L has been defined as screening cut-off for carbapenemase production. Breakpoints for *M. morganii*, *Proteus* spp. and *Providencia* spp. are S ≤ 0.125 mg/L and R >4 mg/L
Meropenem	**0.125**-**0.25**-0.5-1-**2**-4-**8**-16	A	>0.125 mg/L has been defined as screening cut-off for carbapenemase production.
Mero-vaborbactam	**0.125**-**0.25**-0.5-1-**2**-4-8-16	C	ECOFF has not yet been defined. Used to infer class A carbapenemases in isolates that are resistant to carbapenems. For The concentration of vaborbactam is fixed at 8 mg/L.
Ertapenem	**0.06**-**0.125**-**0.25**-0.5-1-**2**-4	A	>0.125 mg/L has been defined as screening cut-off for carbapenemase production. ECOFF has not yet been defined.

Bold: minimum no. of concentrations that are recommended to be included in the study of susceptibility testing; Underlined: ECOFF values (when lacking is due to the absence of definition by EUCAST). When different ECOFFs exist for the different enterobacterial species, the *E. coli* ECOFF is indicated; Light: I category; Dark gray: R category

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Antimicrobial susceptibility testing: automatic systems

Antibiotics and concentrations recommended for the susceptibility testing of *Pseudomonas* spp.

Antimicrobial	Concentrations (mg/L)	Category	Comments
Ticarcillin	8-**16**-**32**-64	E	Breakpoints based on high dose therapy. Not currently used but useful for the inference of resistance mechanisms such as acquired β-lactamases and/or efflux pump overexpression. ECOFF has not yet been defined.
Piperacillin	4-**8**-**16**-**32**-64	C	Breakpoints based on high dose therapy.
Piper-tazobactam	4/4-**8/4**-**16/4**-**32/4**-64/4	A	Breakpoints based on high dose therapy. The concentration of tazobactam is fixed at 4 mg/L.
Ceftazidime	1-**2**-**4**-**8**-**16**-32	A	Breakpoints based on high dose therapy.
Cefepime	1-**2**-**4**-**8**-**16**-32	A	Breakpoints based on high dose therapy.
Ceftolozane-tazob	0.25/4-0.5/4-**1/4**-**2/4**-**4/4**-**8/4**-16/4	C	Useful for the detection of resistance mechanisms, particularly acquired β-lactamases. The concentration of tazobactam is fixed at 4 mg/L.
Cefta-avibactam	0.5/4-1/4-**2/4**-**4/4**-**8/4**-**16/4**-32/4	C	ECOFF has not yet been defined. Useful for the detection of resistance mechanisms, particularly acquired β-lactamases.
Aztreonam	**1**-**2**-**4**-**8**-**16**-32	A	Breakpoints based on high dose therapy. Useful for the detection of resistance mechanisms such as acquired MBLs.
Imipenem	0.5-**1**-**2**-**4**-**8**-16	A	Breakpoints based on high dose therapy.
Meropenem	0.25-0.5-**1**-**2**-**4**-**8**-16	A	
Mero-vaborbactam	**0.125**-**0.25**-**0.5**-**1**-**2**-4-8-16	C	ECOFF has not yet been defined. The concentration of vaborbactam is fixed at 8 mg/L.

Bold: minimum no. of concentrations that are recommended to be included in the study of susceptibility testing; Underlined: ECOFF values (when lacking is due to the absence of definition by EUCAST). When different ECOFFs exist for the different enterobacterial species, the *E. coli* ECOFF is indicated; Light: I category; Dark gray: R category

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Antimicrobial susceptibility testing: automatic systems

Antibiotics and concentrations recommended for the susceptibility testing of *Stenotrophomonas maltophilia*

Antimicrobial agent		Concentrations (mg/L)	Category	Comments
ß-lactams	Imipenem	0.5-**1**-**2**-**4**-**8**-16	E	*S. maltophilia* is intrinsically resistant to all β-lactams. Imipenem MIC values >8 mg/L supports identification.
Fluoroquinolones	Levofloxacin	0.25-0.5-**1**-**2**-**4**-**8**	A	ECOFF has not yet been defined. Breakpoints have not been defined by EUCAST, those shown are recommended by COESANT
Tetracyclines	Minocycline	1-2-**4**-**8**-**16**	A	Breakpoints have not been defined by EUCAST, those shown are recommended by COESANT
Others	Cotrimoxazole	1/19-**2/28**-**4/76**-**8/152**	A	

Bold: minimum number of concentrations that are recommended to be included in the study of susceptibility testing
Underlined: ECOFF value (when lacking is due to the absence of definition of this value by EUCAST).
Light grey: I category; Dark gray: R category

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Antimicrobial susceptibility testing: automated/semi-automated systems

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Review article

Recommendations of the Spanish Antibiogram Committee (COESANT) for selecting antimicrobial agents and concentrations for *in vitro* susceptibility studies using automated systems

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eimc Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica

gemara Grupo de Estudio de los Mecanismos de Acción y de la Resistencia a los Antimicrobianos

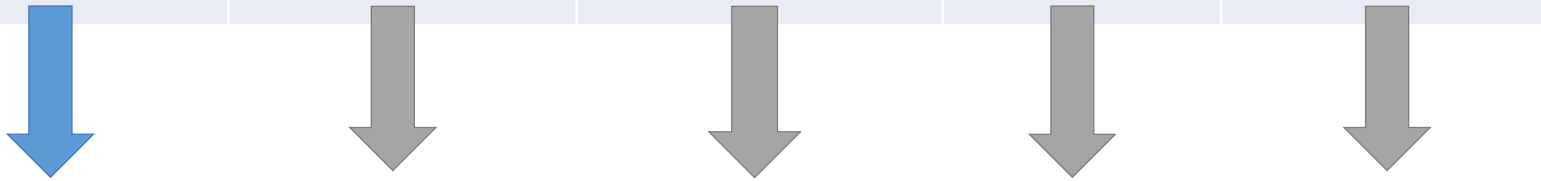
CoESAnt

Plan Nacional Resistencia Antibióticos

agencia española de medicamentos y productos sanitarios

New phenotypic AST methods

	FASTinov	Qlinea / Thermo Fisher	Specific/ Biomerieux	Accelerate Dx	dRAST
Time to AST results	2 h	6 h	5.5 h (Avg)	7 h	4-5 h
No. of antibiotics tested	GN: 13 GP: 8	GN: 23 GP: --	GN: GP:	GN: 12 GP: 5	GN: 17 GP: 18
Throughput (1 instrument)	5 AST in 4 h 12 AST in 8 h	0 AST in 4 h 12 AST in 8 h	0 AST in 4 h 4 AST in 8 h	0 AST in 4 h 1 AST in 8 h	12 AST in 4-5 h
Usability (hands-on-time)	10’	2’	2’:30’’	2’	1’



2h AST category

rapid AST category

AST with TTR 2h
Same day

“Rapid” AST with TTR 6-8 hours
Results might be delivered *next day*

CoEsAnt

Documento CoEsAnt: antimicrobianos en paneles comerciales

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