Automatisation totale en bactériologie diagnostique : réalité ou fantaisie ?

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Laboratoire de Bactériologie

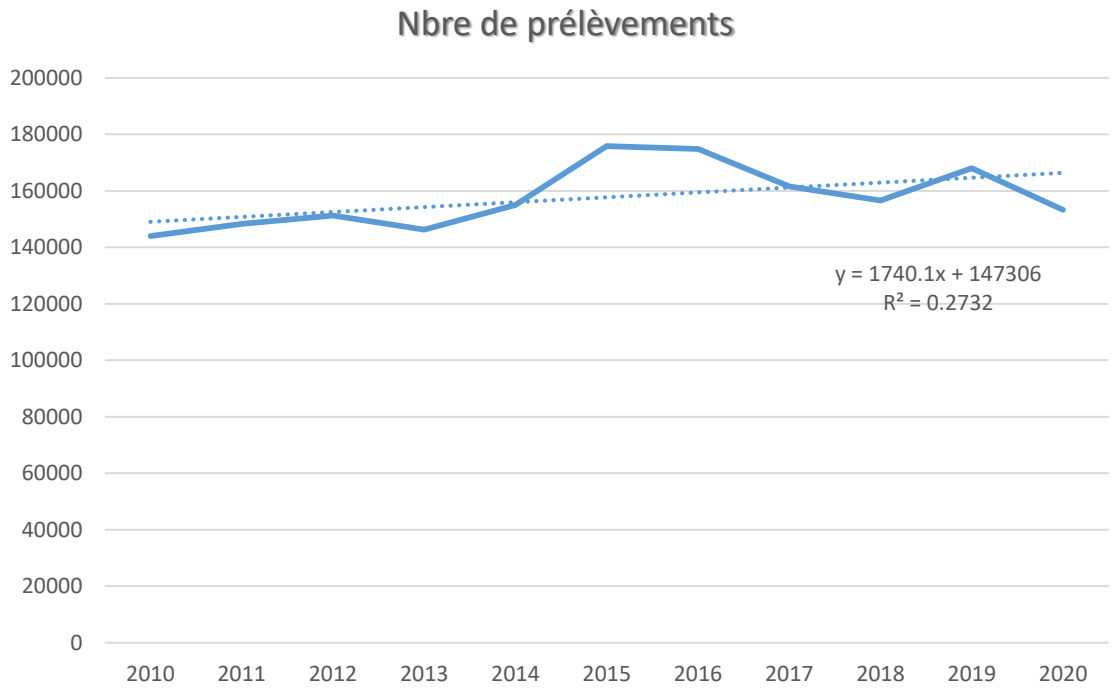
Hôpitaux Universitaires Genève

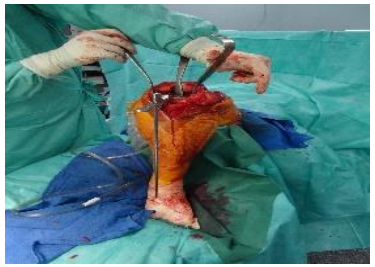
ccCTA - 17 septembre 2021

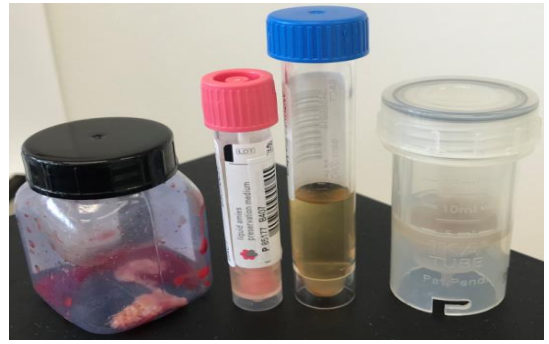
There is no conflict of interest

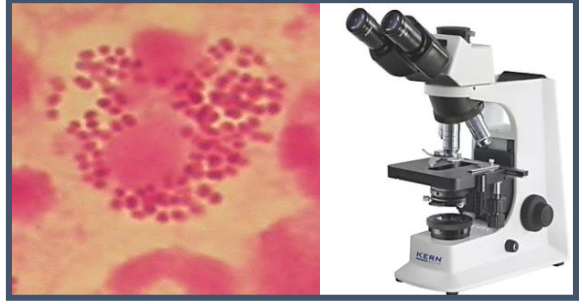
- Conventional diagnostic work-up
- MALDI-TOF/MS
- Total Laboratory Automation
- Fully Automated solution for Antimicrobial Disk Diffusion Susceptibility Testing

Laboratoire de Bactériologie
Hôpitaux universitaires de Genève

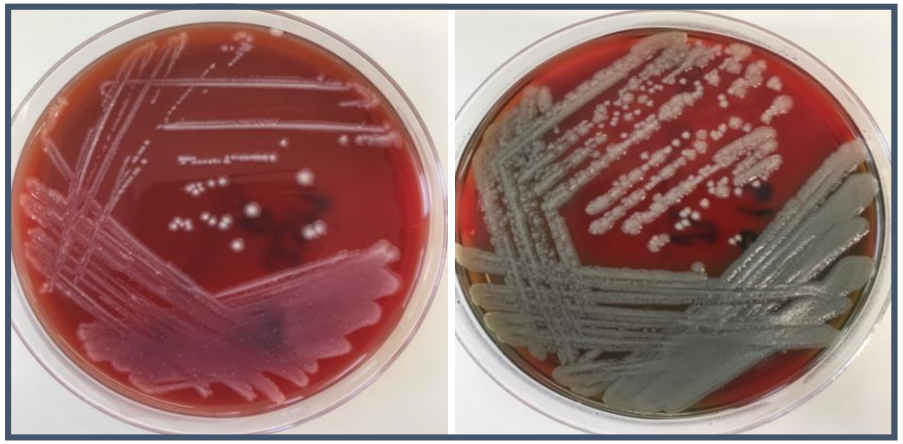








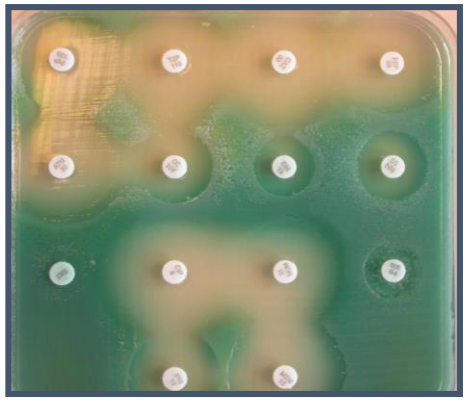
H0



H48
Pathogens
ID and AST
results

Biochemistry testing methods for identifying microorganisms
(time consuming and complex tasks)

Antimicrobial
Disk Diffusion
Susceptibility
Testing



Conventional diagnostic work-up

These routine laboratory techniques ensure an accurate identification of most microorganisms

BUT

- Costly 
- require time 

Conventional diagnostic work-up

STEP-1: Gram stain, samples inoculation on different culture media and incubation

> 1000 culture media per day / 4 Technologist (full time)

Conventional diagnostic work-up

STEPs 2 to 4: Incubation of culture media plates, Reading and Microbial identification

> 2000 culture media per day

Conventional diagnostic work-up

STEP-5: Antimicrobial susceptibility testing

> 100 AST per day / 1 Technologist (full time)

Journal of *Clinical Medicine*

MDPI

Article

Mortality After Delay of Adequate Empiric Antimicrobial Treatment of Bloodstream Infection

Merel M. C. Lambregts [1,*,†], Roos Wijnakker [1,†], Alexandra T. Bernards [2], Leo G. Visser [1], Saskia le Cessie [3] and Mark G. J. de Boer [1]

Adequacy of Early Empiric Antibiotic Treatment and Survival in Severe Sepsis: Experience from the MONARCS Trial

Rodger D. MacArthur,[1] Mark Miller,[2] Timothy Albertson,[3] Edward Panacek,[3] David Johnson,[4] Leah Teoh,[5] and William Barchuk[5]

[1]Wayne State University, Detroit, Michigan; [5]Abbott Laboratories, Parsippany, New Jersey; [3]University of California, Davis, Sacramento, California; and [2]McGill University, Montreal, and [4]Department of Medicine, Royal University Hospital, Saskatoon, Canada

As part of the Monoclonal Anti-TNF: A Randomized Controlled Sepsis (MONARCS) trial, which enrolled patients with suspected sepsis, we sought to determine whether adequate antibiotic therapy was associated with a decreased mortality rate. The study enrolled 2634 patients, 91% of whom received adequate antibiotic therapy. The mortality rate among patients given adequate antibiotic treatment was 33%, versus 43% among patients given inadequate treatment ($P < .001$). We conclude that adequate antibiotic therapy results in a significant decrease in the crude mortality rate among patients suspected of sepsis.

AAC Journals.ASM.org

Impact of Inadequate Empirical Therapy on the Mortality of Patients with Bloodstream Infections: a Propensity Score-Based Analysis

Pilar Retamar,[a] María M. Portillo,[a] María Dolores López-Prieto,[b] Fernando Rodríguez-López,[c] Marina de Cueto,[a] María V. García,[d] María J. Gómez,[e] Alfonso del Arco,[f] Angel Muñoz,[g] Antonio Sánchez-Porto,[h] Manuel Torres-Tortosa,[i] Andrés Martín-Aspas,[j] Ascensión Arroyo,[k] Carolina García-Figueras,[b] Federico Acosta,[l] Juan E. Corzo,[m] Laura León-Ruiz,[n] Trinidad Escobar-Lara,[o] Jesús Rodríguez-Baño,[a,p] and the SAEI/SAMPAC Bacteremia Group

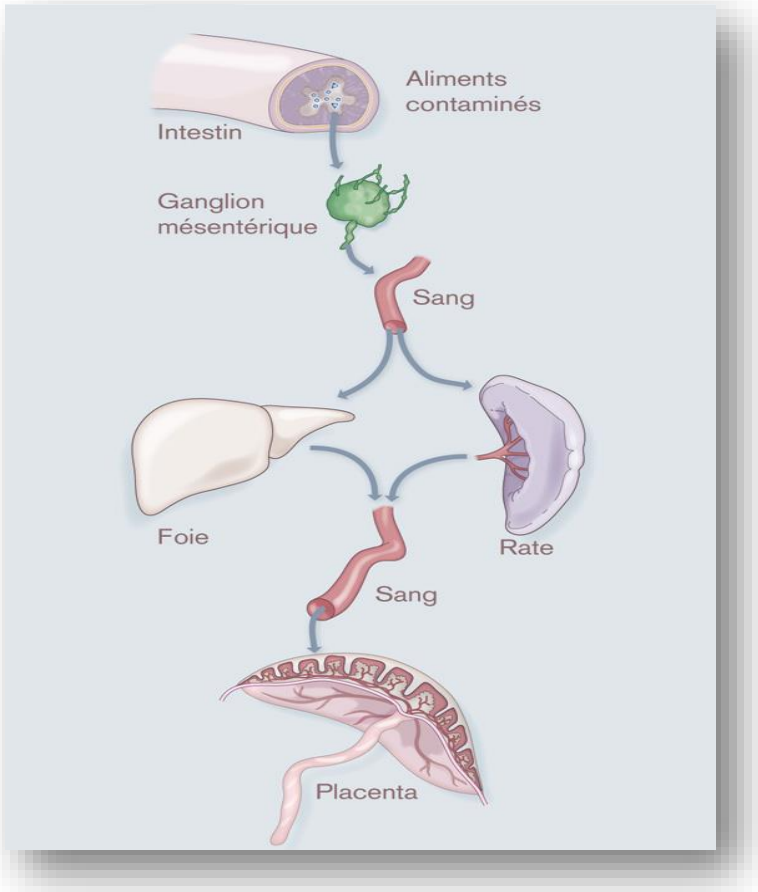
JCM
Journals.ASM.org

LETTER TO THE EDITOR

Misidentification of *Listeria monocytogenes* by the Vitek 2 System

Niall De Lappe, Ciara Lee, Jean O'Connor, Martin Cormican

National *Salmonella*, *Shigella* & *Listeria* Reference Laboratory, Medical Microbiology Department, University Hospital Galway, Galway, Ireland



Pizarro-Cerda et al. Cell 2006

Brucellose acquise au laboratoire

Inde

Patient aux urgences avec drainage d'un abcès pleural

- Envoi du prélèvement au labo sans autre indication
- Inoculation des milieux de culture en class 2 biosafety
- Absence de germe au Gram
- 72h, croissance de cocobacilles à Gram négatif
- Identification API 20 NE panel (BioMérieux):
  Moraxella phenylpyruvica

Après 22 jours, identification définitive pour *Brucella* !!!

26 personnes travaillant dans laboratoire

19 physiquement présent

1 a « reniflé » les milieux de culture

6 ont manipulé (dont une femme enceinte)

Table 1. Serum titers of *Brucella melitensis* in exposed laboratory personnel (exposure between 27 June to 9 July).

Laboratory worker	Prophylaxis received	Observed titer(s)[a]							
		11 Jul	25 Jul	8 Aug	22 Aug	5 Sep	19 Sep	3 Oct	17 Oct
1	No	0	…	0	…	0	…	…	0
2 (HRI	No	0	…	0	1:80; <1/160	1:320[c]; 1:1280[c]	…	…	…

[Prevention of Laboratory-Acquired Brucellosis. CID 2004; 38: 119]

MALDI-TOF/MS

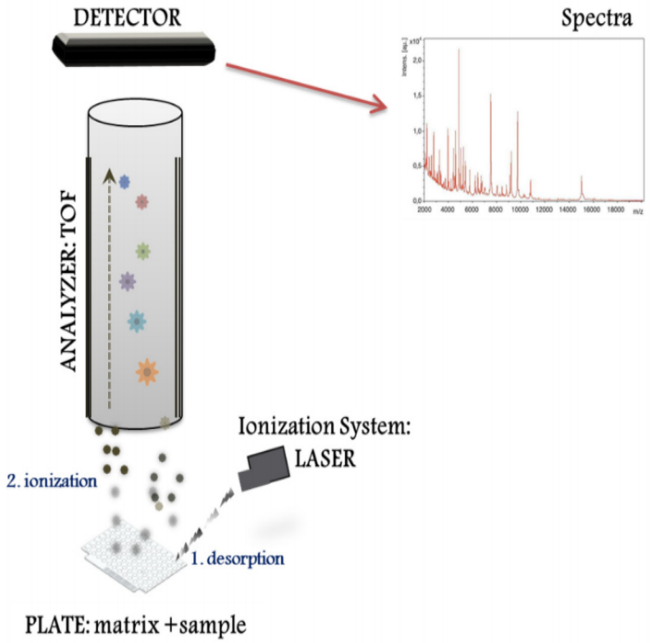
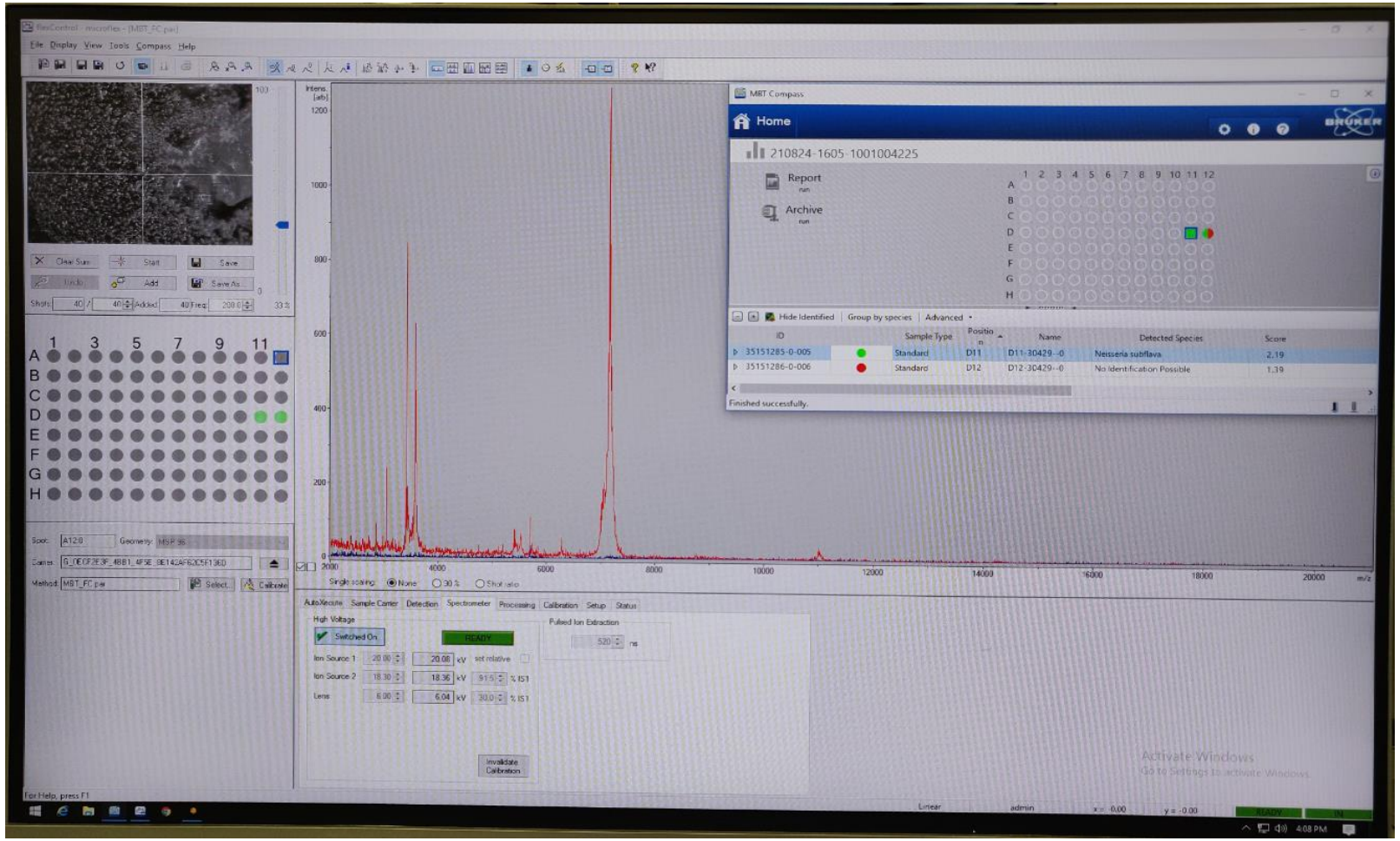
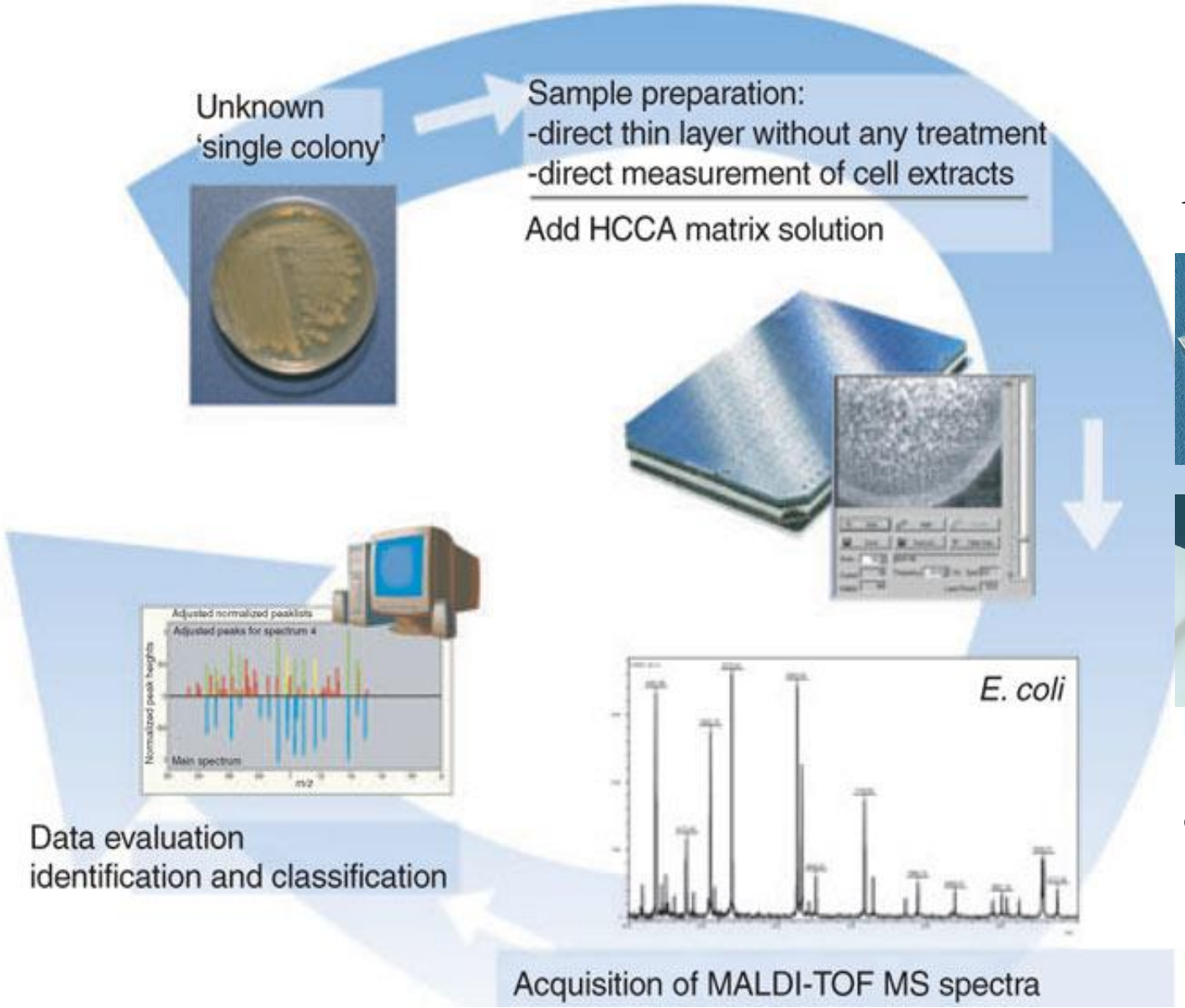
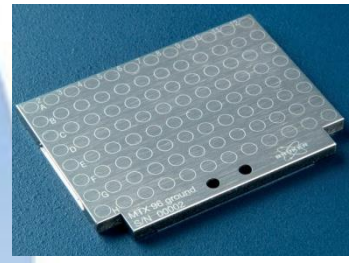


Figure 1. Schema showing the linear mode workflow in a MALDI–TOF MS system.





Put one colony
on the target
And add a matrix



Insert the target
and start shooting

HCCA: alpha-Cyano-4-hydroxycinnamic acid

JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2010, p. 1169–1175 Vol. 48, No. 4
0095-1137/10/$12.00 doi:10.1128/JCM.01881-09

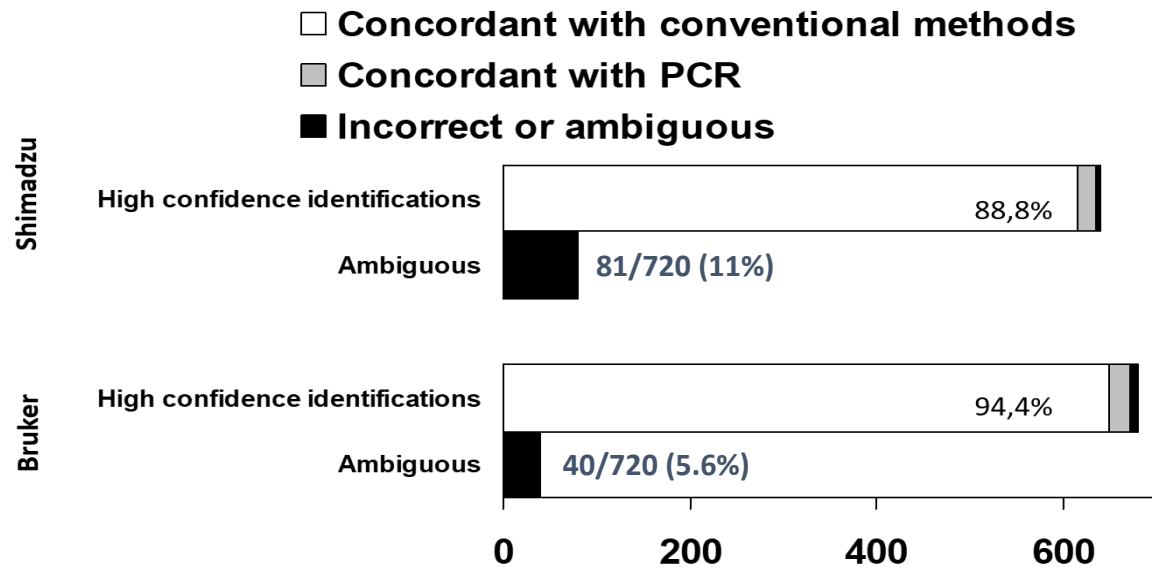
Comparison of Two Matrix-Assisted Laser Desorption Ionization–Time of Flight Mass Spectrometry Methods with Conventional Phenotypic Identification for Routine Identification of Bacteria to the Species Level[▽]

Abdessalam Cherkaoui,[1]* Jonathan Hibbs,[2] Stéphane Emonet,[1] Manuela Tangomo,[2] Myriam Girard,[2] Patrice Francois,[2] and Jacques Schrenzel[1,2]

Clinical Microbiology Laboratory[1] and Genomic Research Laboratory,[2] Service of Infectious Diseases, University of Geneva Hospitals (HUG), CH-1211 Geneva 14, Switzerland

Received 23 September 2009/Returned for modification 23 November 2009/Accepted 9 February 2010

Accuracy of MALDI-TOF MS identifications of 720 clinical isolates



Cost and timeliness estimates of Bruker-based identification

	Cost per isolate ($US) Avg.	Cost per isolate ($US) Total	Turnaround time (hr) Avg.	Turnaround time (hr) Total
High confidence MALDI-TOF MS (n=636)	$0.50	$318	0.08	53
Lower-confidence and Ambiguous MALDI-TOF MS (n=84)	$10.50	$882	24	2,016

Total cost: $1,200 **Average time: 3 hrs**

Cost and timeliness estimates of conventional identification

	Cost per isolate ($US) Avg.	Cost per isolate ($US) Total	Turnaround time (hr) Avg.	Turnaround time (hr) Total
***E. coli* (n=216)**	$0.20	$43	1	216
***S. aureus* (n=55)**	$1.50	$83	1	55
Other (n=449)	$10.00	$4,490	24	10,776

All isolates (n=720) **Total cost: $4,616** **Average time: 15 hrs**

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2011, p. 3004–3005 Vol. 49, No. 8
0095-1137/11/$12.00 doi:10.1128/JCM.00240-11

Evaluation of Matrix-Assisted Laser Desorption Ionization–Time of Flight Mass Spectrometry for Rapid Identification of Beta-Hemolytic Streptococci[▽]

Abdessalam Cherkaoui,[1]* Stéphane Emonet,[1] José Fernandez,[1] Didier Schorderet,[1] and Jacques Schrenzel[1,2]

Bacteriology Laboratory[1] and Genomic Research Laboratory, Department of Internal Medicine,[2] Service of Infectious Diseases, University of Geneva Hospitals (HUG), CH-1211 Geneva 14, Switzerland

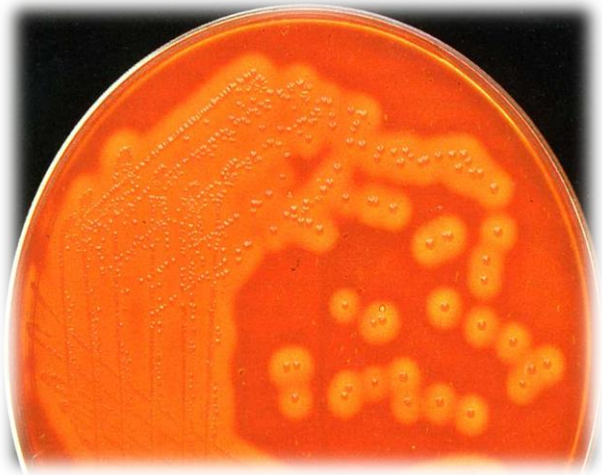
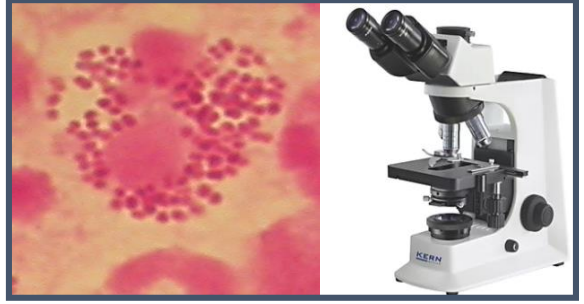
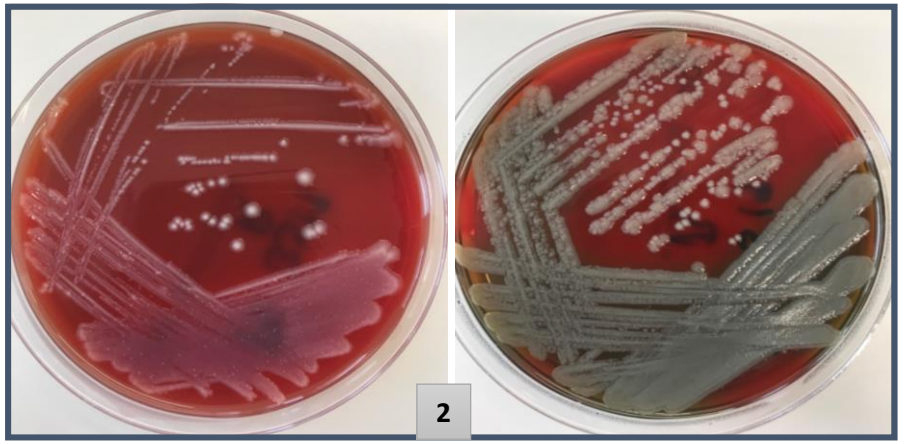


TABLE 1. Accuracy of MALDI-TOF MS identification of 386 beta-hemolytic streptococcal isolates[a]

Organism group (no. of isolates) and identification parameter	No. of isolates (%) found by: MALDI-TOF MS identification with score of >2.0	Vitek2 identification	16S rRNA gene sequencing
Streptococcus pyogenes (52)			
Species correct	52 (100)	48 (92)	4 (7.7)
Major error	0	2 (3.8)	
Minor error	0	0	
No identification	0	2 (3.8)	
Streptococcus agalactiae (306)			
Species correct	306 (100)	269 (88)	37 (12)
Major error	0	2 (0.7)	
Minor error	0	32 (10.5)	
No identification	0	3 (1.0)	
Streptococcus dysgalactiae (28)			
Species correct	28 (100)	11 (39)	17 (6.1)
Major error	0	7 (25)	
Minor error	0	1 (3.6)	
No identification	0	9 (32)	

H0

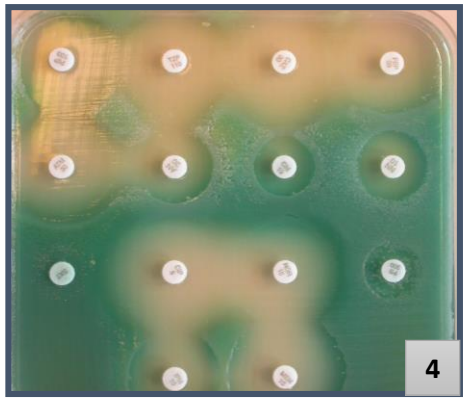


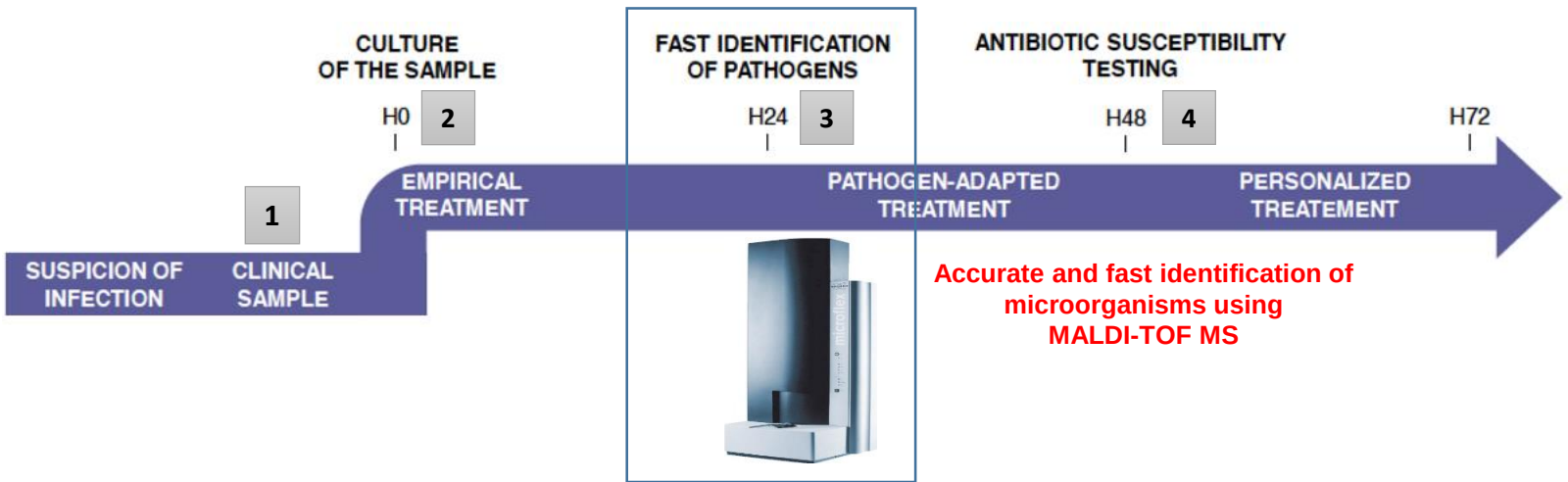


H48
Pathogens
ID and AST
results

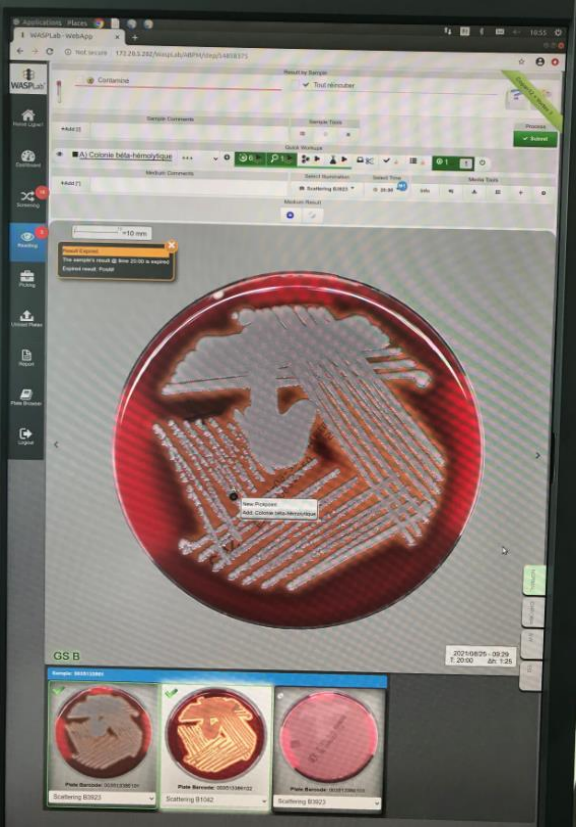
Biochemistry testing methods for identifying microorganisms (time consuming and complex tasks)

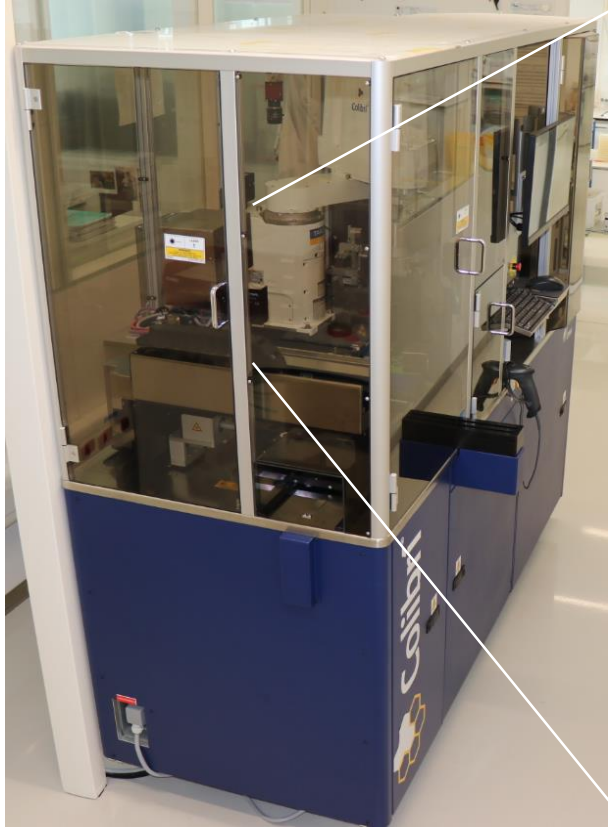
Antimicrobial Disk Diffusion Susceptibility Testing

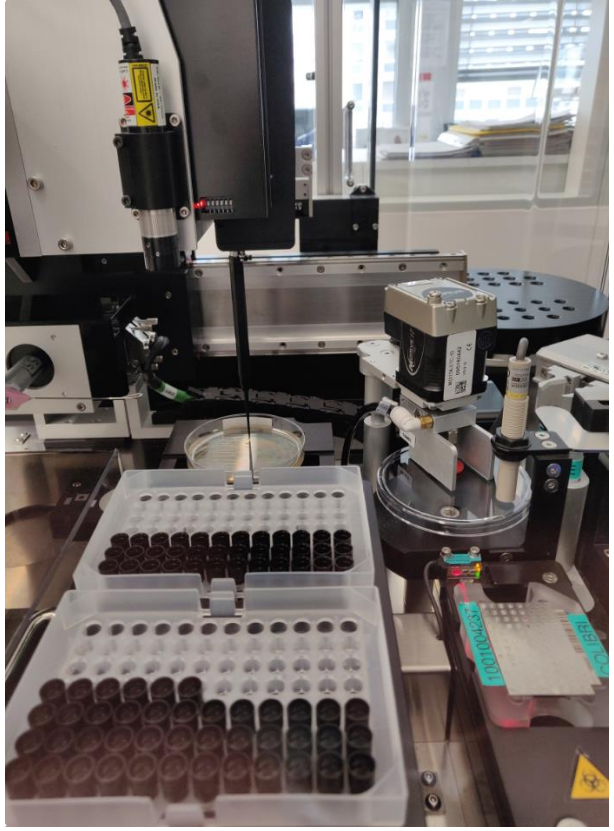




Accurate and fast identification of microorganisms using MALDI-TOF MS





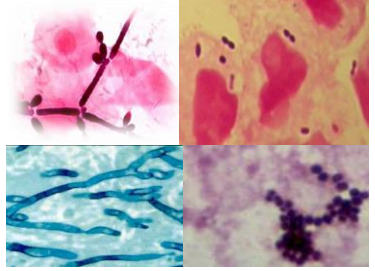


Automatic System for Colony Picking and MALDI-TOF Targets Preparation

Applications of MALDI-TOF mass spectrometry in clinical microbiology

- MALDI-TOF MS to identify rare pathogenic bacteria
- MALDI-TOF MS directly from positive blood culture - rapid identification protocols
- MALDI-TOF MS directly from urine samples
- MALDI-TOF-based subtyping as a tool for outbreak investigation
- Antibiotic resistance testing using MALDI-TOF MS
- …

Total Laboratory Automation (TLA)



Step-1

Step-2

Step 1 Inoculation

Step 2 Incubation

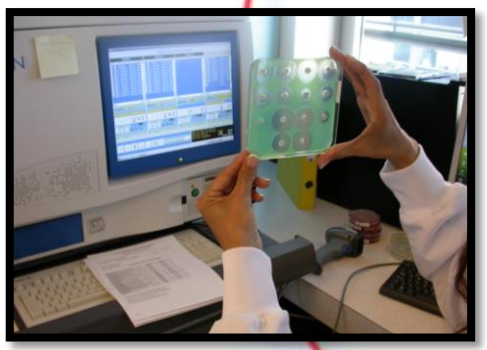
Step 3 Reading

Step 4 Identification

Step 5 DD AST

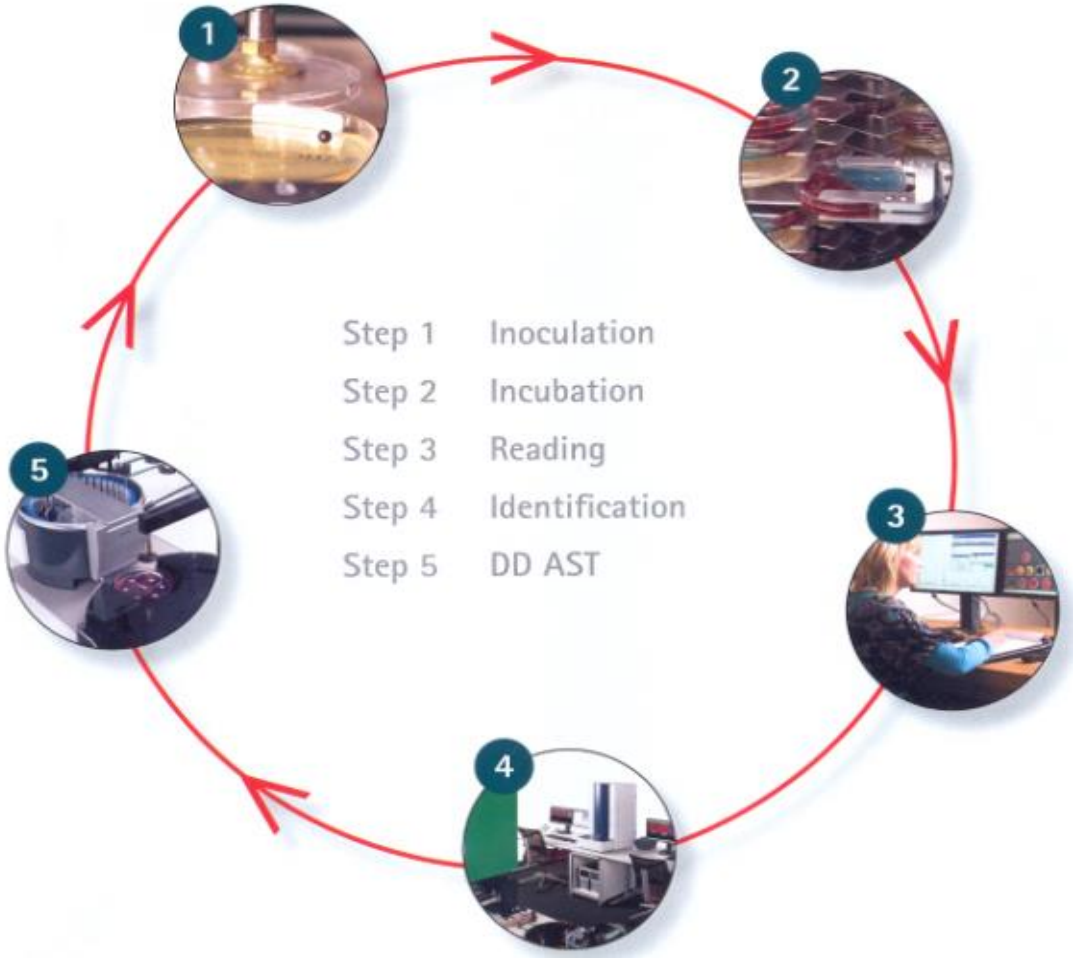
Step-3

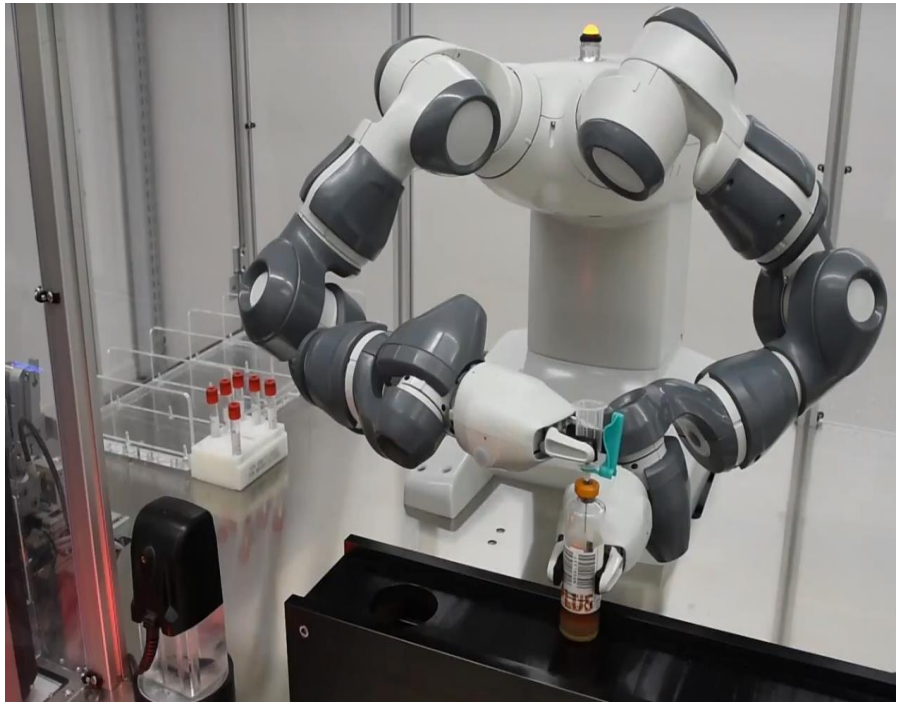
Step-4



Step-5

The beginning of great changes in the Bacteriology Lab





Copan Diagnosis, Inc. www. Copanusa.com

DEONET factory, the Netherlands (Fot. ABB)

www.chroniclelive.co.uk

Progressive automation of Microbiology culture-based testing

Preanalytical specimen management and processing : inoculation and steaking

Total Laboratory Automation : clinical specimens processing, Incubation and culture media plates digital imaging

The BD Kiestra™ InoqulA+
*2006

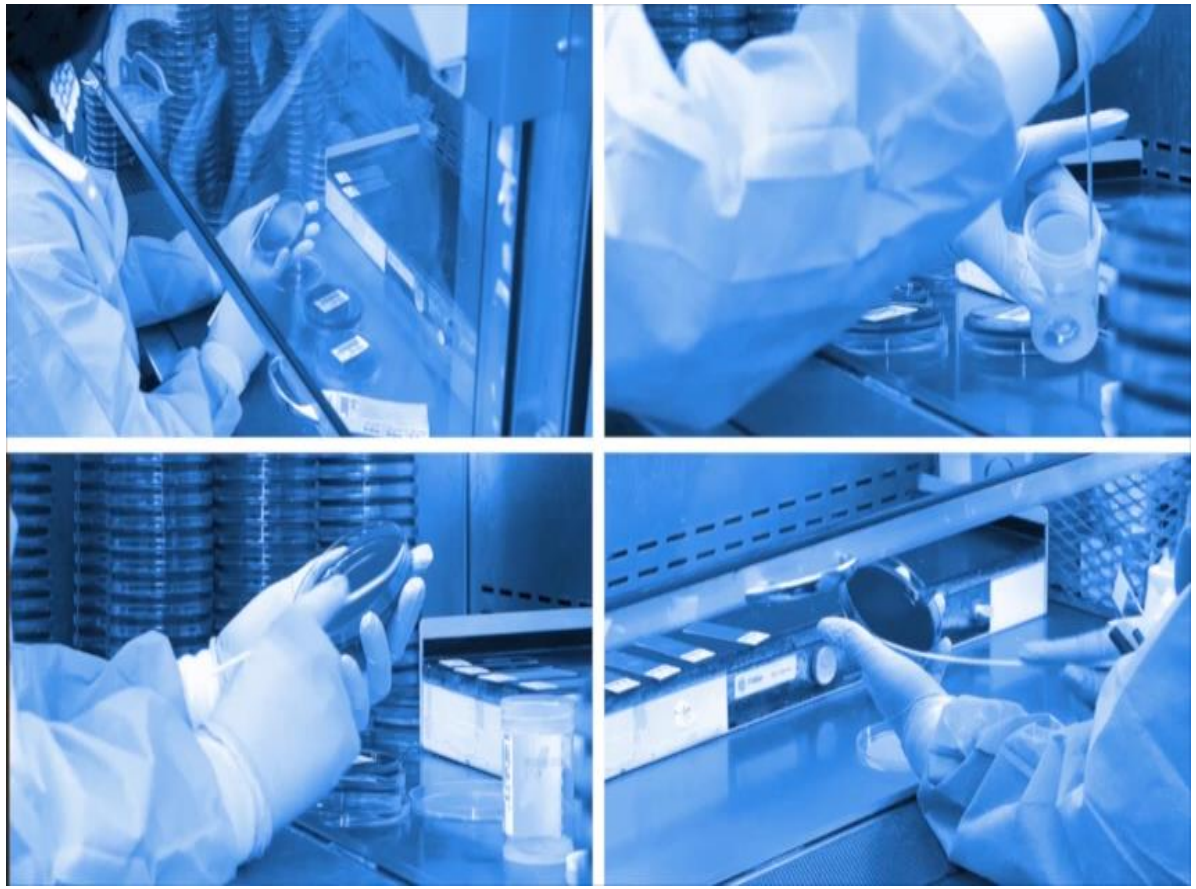
The BD Kiestra™ WCA system
*2012

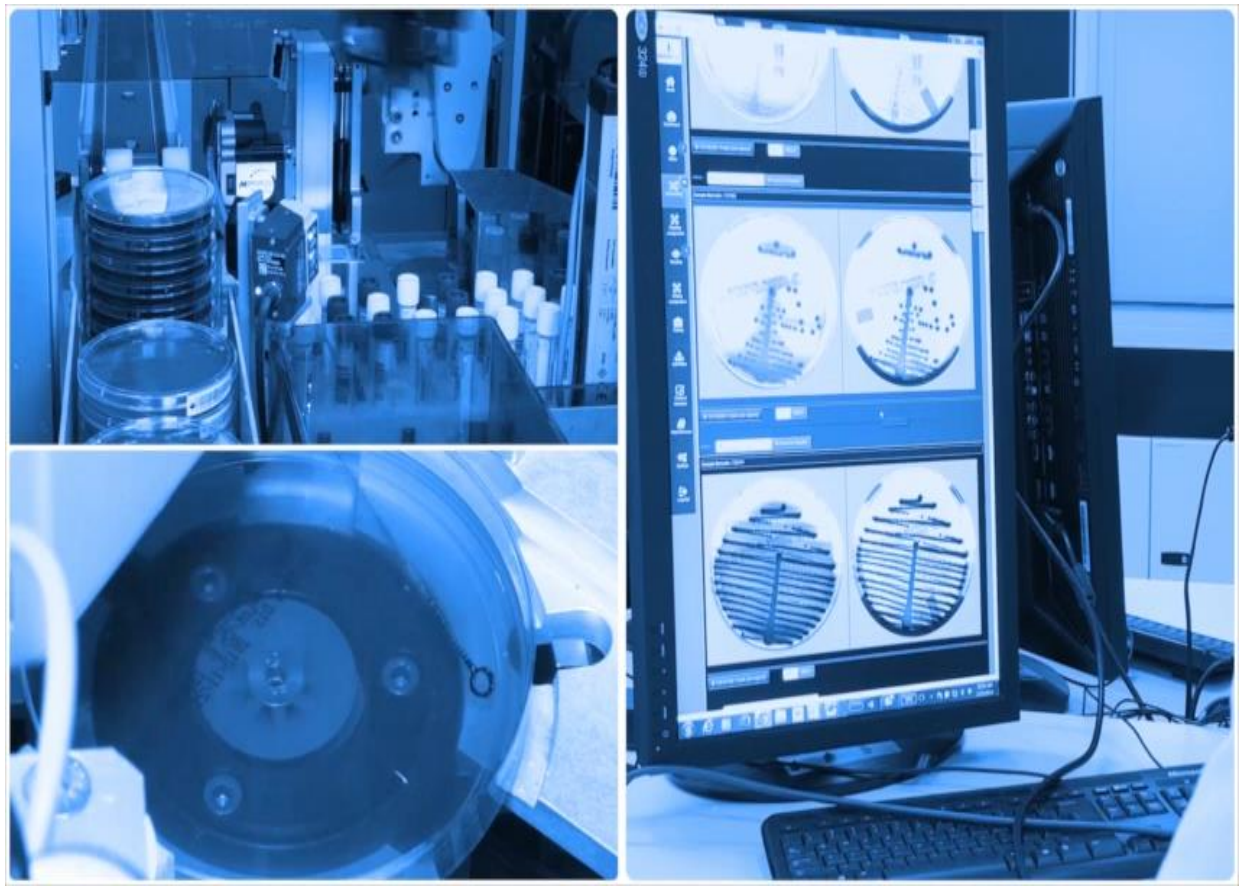
The BD Kiestra™ TLA system
*2006

Copan WASP / *2006

CopanWASPLab
*2012

*First installation in routine diagnostic laboratory



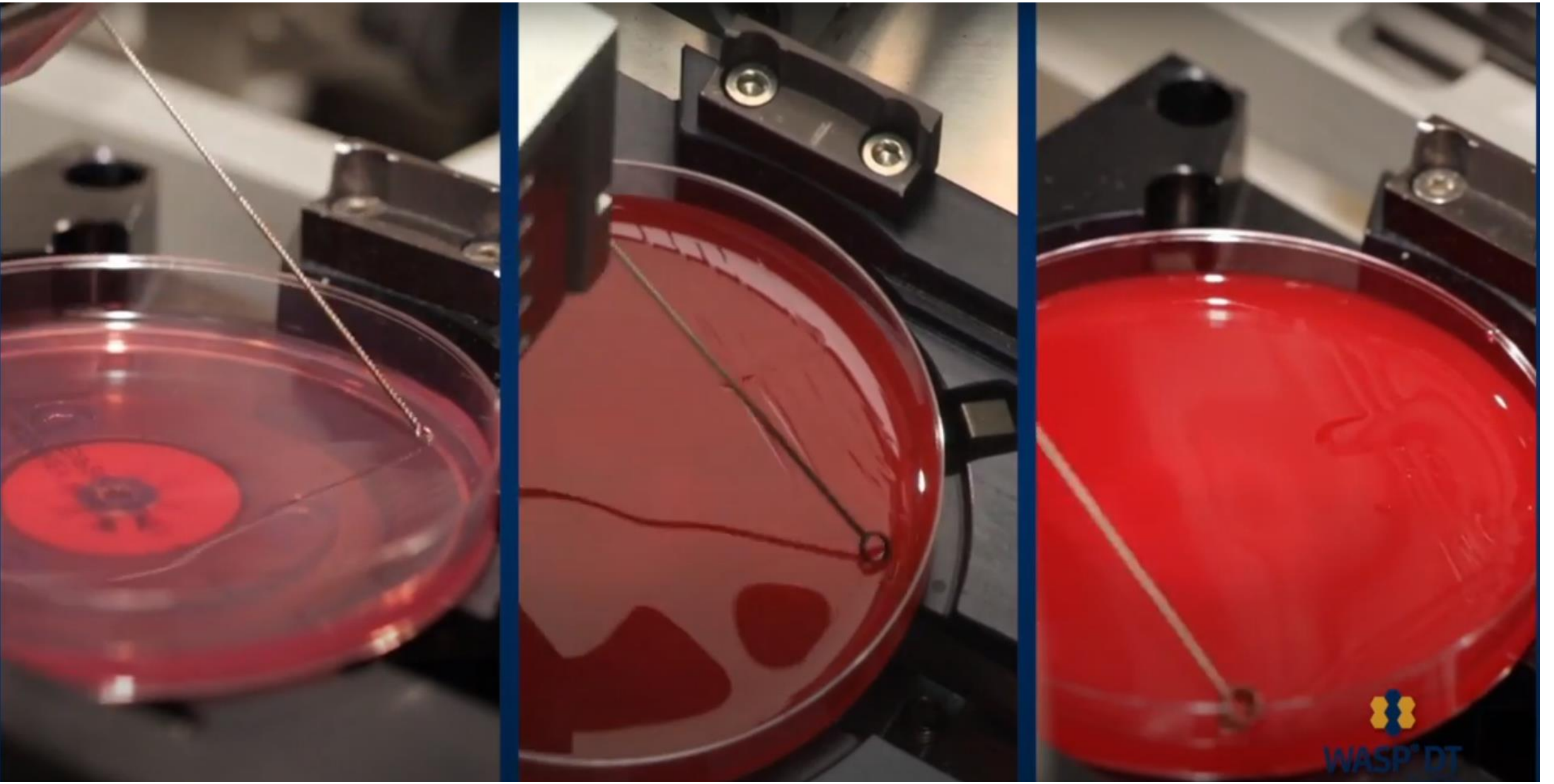


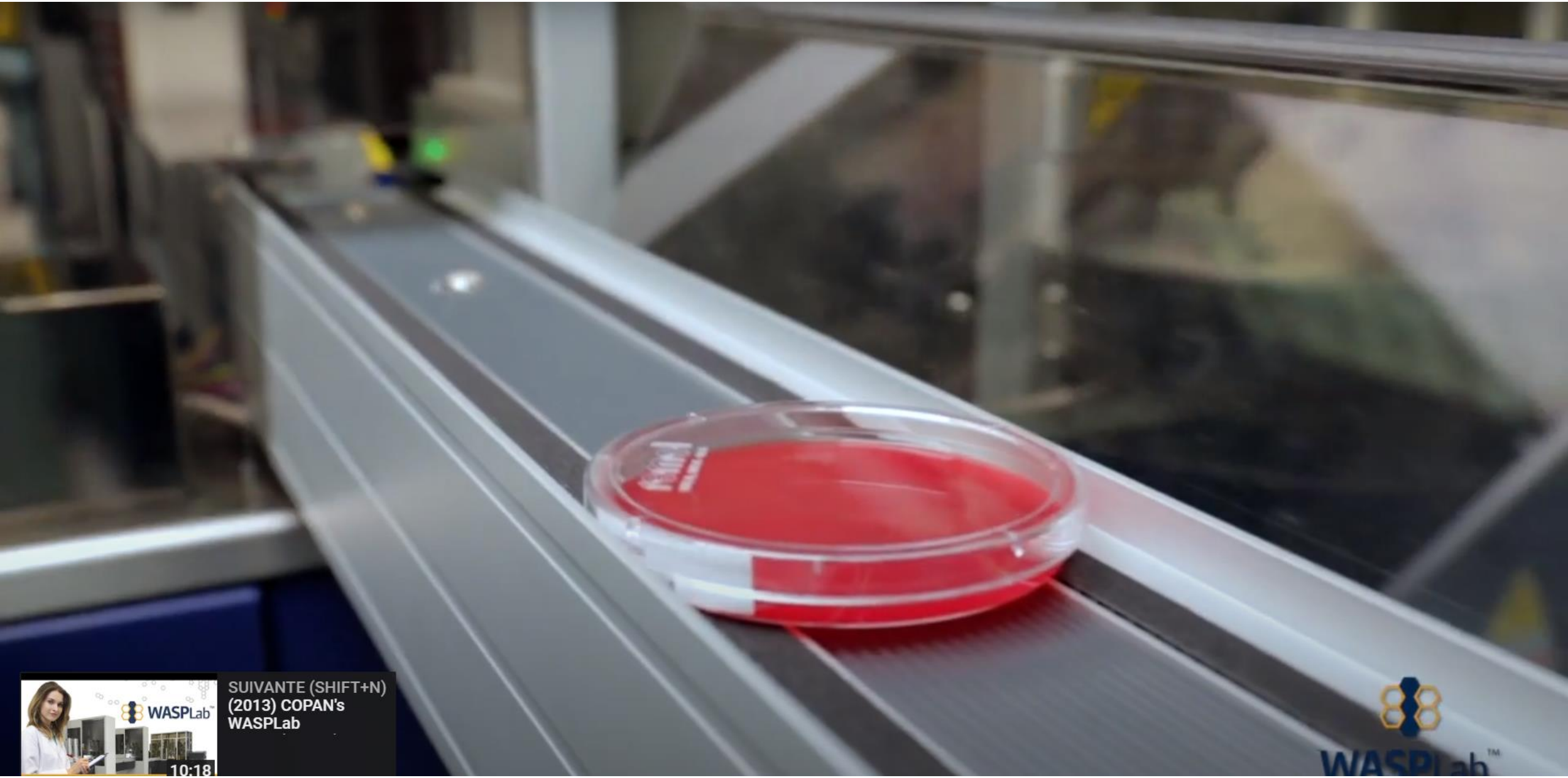
Traditional Manual Process

Fully Automated Process

(Courtesy M. Savarese, Copan)


WASP
Gram Slide Preparation


WASP DT


WASPLab™
SUIVANTE (SHIFT+N)
(2013) COPAN's WASPLab
10:18
WASPLab™


Individual plate shelves
ensure homogenous
environmental conditions
and excellent
thermal conductivity

At the image acquisition station a
critical zero-hour image is recorded

TLA : Project management and change management

Project initiation: defining needs

Project release: drafting tender

Phase release: Lab installation and IT

System delivery (September 2018)

Routine launch of the first system (November 2018)

CURRENT 2016

- Determination of the context and objectives
- Business plan
- Pre-study stage
- Project chart
- Project organization
- Validation of the dedicated budget

CURRENT 2017

- Visits of five automated microbiology labs in Europe
- Upstream assessment and definition of needs
- Writing of a comprehensive tender
- Call for tender
- Tenders presentations
- Selection of an automated system
- Lab workflow analyses
- Official system order

1st SEMESTER 2018

- Architectural and technical adaptation of the laboratory
- Defining detailed WASPLab specifications
- LIS interface development

2nd SEMESTER 2018

- WASPLab installation and activation
- System configuration
- Testing
- First validation projects
- Training of lab technologists

2019

- Sequential implementation of sample types
- Sequential validation projects
- Completion of the training
- Change management
- Continuous process and workflow improvement

Figure 1 Automation of the clinical bacteriology laboratory at Geneva University Hospitals: Specific steps executed and time dedicated to perform each of the project phases.

System-1 is composed of 2 WASP, 2 “CO2 (5%) atmosphere” and 1 “air atmosphere” incubators.
System-2 for AST is composed of 1 WASP, and 1/2 “air atmosphere” incubator.

Cherkaoui et al. (2020) Eur J Clin Microbiol Infect Dis

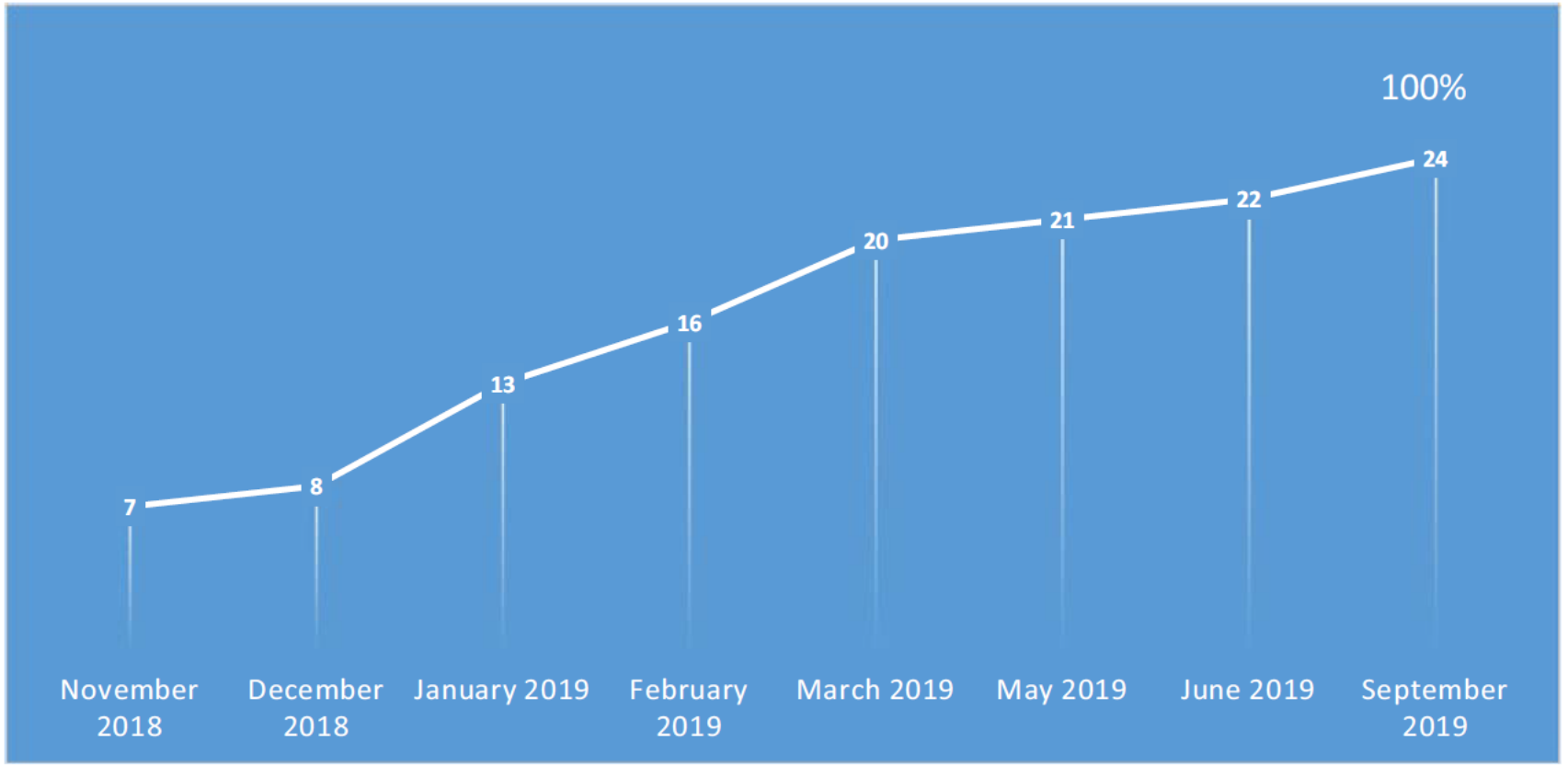


Fig. 2 Number of laboratory technologists trained to perform bacteriology analyses on the WASPLabTM

Cherkaoui et al. (2020) Eur J Clin Microbiol Infect Dis

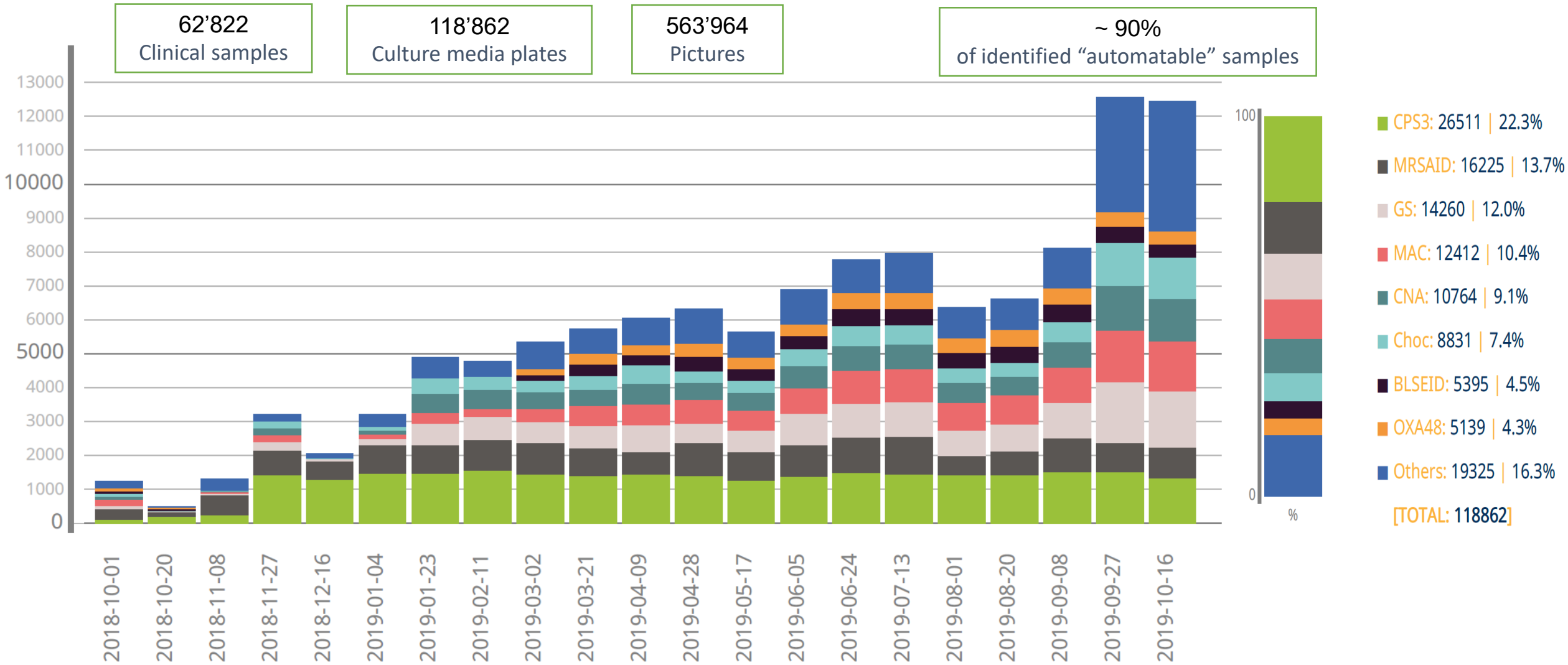
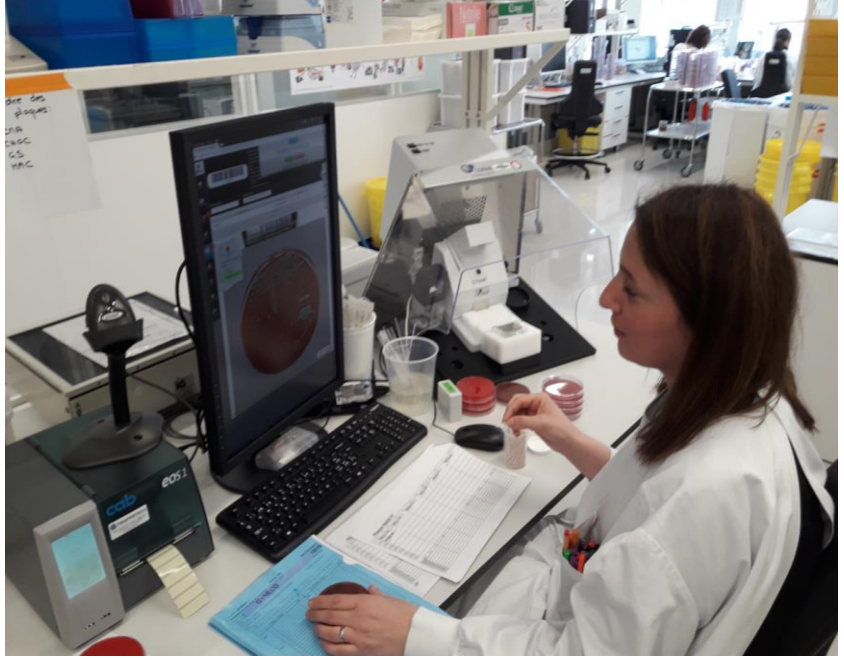


Figure 3 Sequential implementation on the WASPLabTM of the various sample types referred to the bacteriology laboratory at Geneva University Hospitals between October 2018 and October 2019

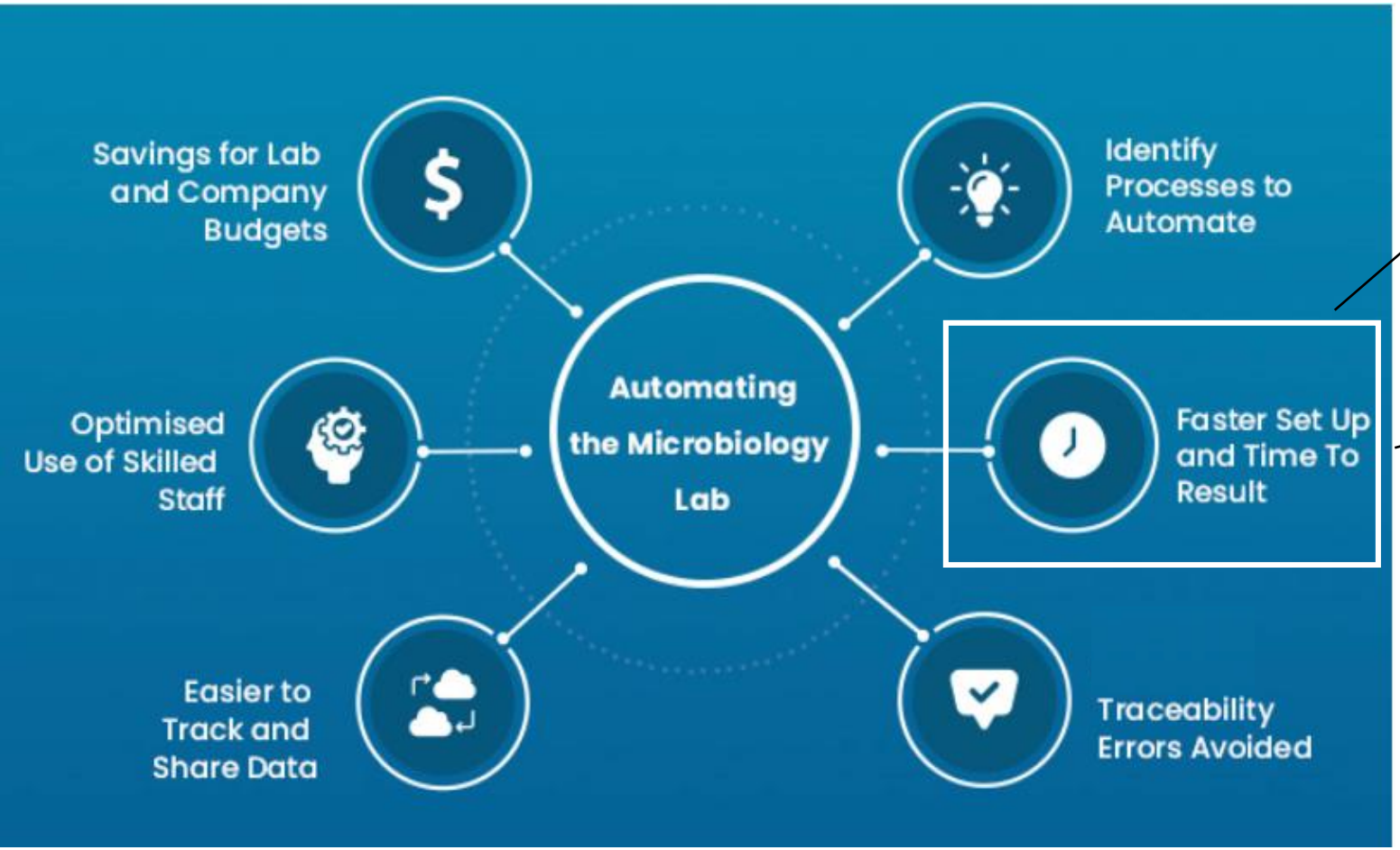
CPS3, CHROMID® CPS® Elite; MRSAID, CHROMID® MRSA; GS, Blood agar; MAC, MacConkey agar; CNA, CNA agar; Choc, Chocolate agar; BLSEID, CHROMID® ESBL; OXA48, CHROMID® OXA-48

Cherkaoui et al. (2020) Eur J Clin Microbiol Infect Dis




WASPLab

Laboratory efficiency improvement



TLA enables the reduction of the incubation times and allows earlier culture readings

Fully Automated solution for AST by **Disk Diffusion**

Clinical Microbiology and Infection 25 (2019) 1430.e5–1430.e12

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Copan WASPLab automation significantly reduces incubation times and allows earlier culture readings

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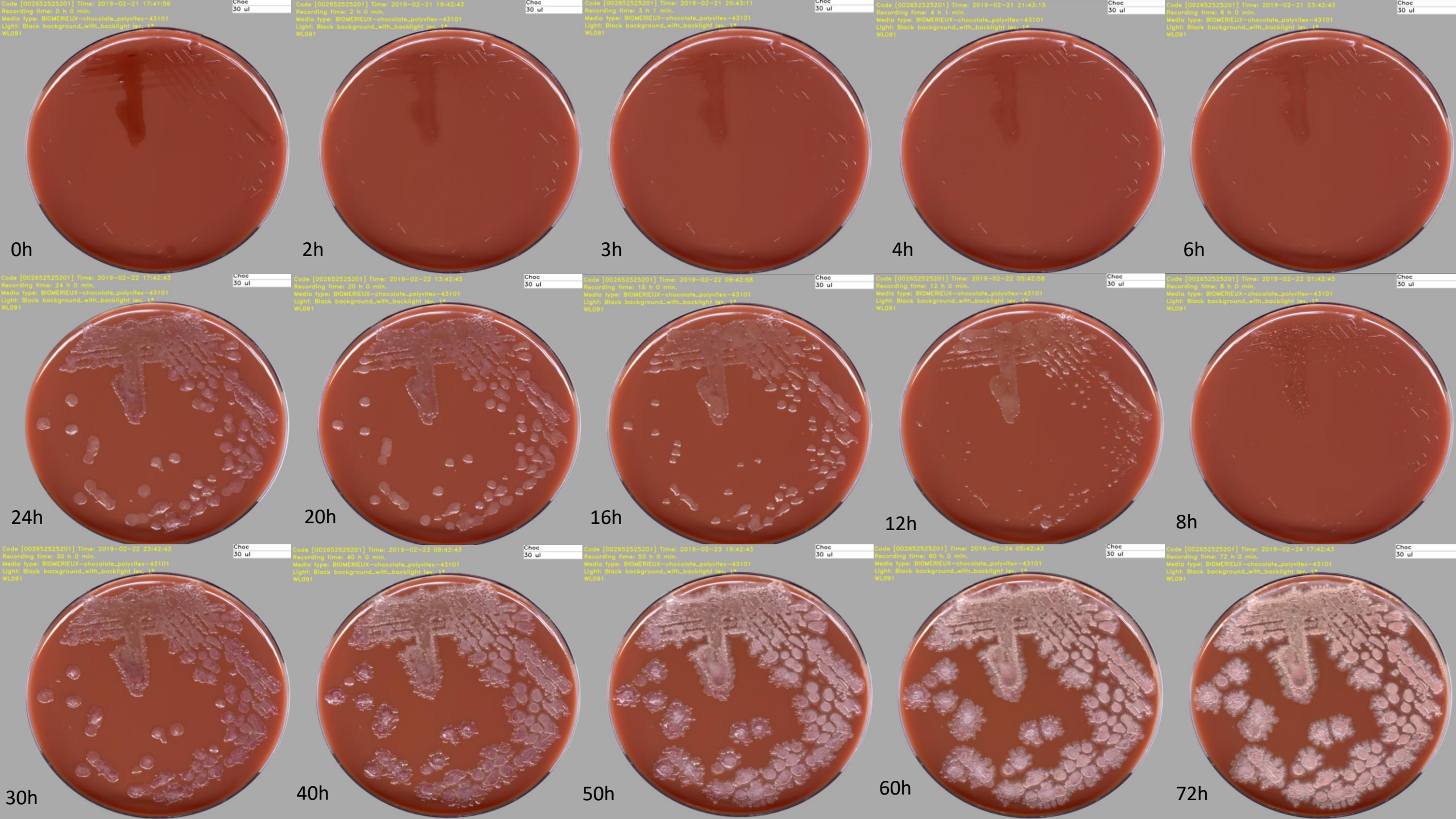
[3] *Division of Laboratory Medicine, Department of Medical Specialities, Faculty of Medicine, Geneva, Switzerland*
[4] *Genomic Research Laboratory, Division of Infectious Diseases, Department of Medical Specialities, Faculty of Medicine, Geneva, Switzerland*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12h
8h
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40h
50h
60h
72h

Table 1: The incubation protocols, the culture media used for each sample type, and the number of samples included in the derivation set and in the independent validation set.

CPE: Carbapenemase-producing Enterobacteriaceae, MRSA : Methicillin-resistant *Staphylococcus aureus* , MSSA: Methicillin susceptible *Staphylococcus aureus* , ESBL : Extended-spectrum beta-lactamases; CNA agar: Colistin-Nalidixic Acid agar

Clinical sample types	WASP coupled to conventional incubation and manual diagnostic		WASPLab	
	Culure media type	Routine incubation period	Number of samples included in the derivation set	Number of samples included in the independant validation set
Urine specimens	CHROMID® CPS® Elite (BioMérieux, Geneva, Switzerland)	18h-24h and 48h	109	266
Genital tract specimens	Blood agar, chocolate agar, CNA agar, and MacConkey agar	24h and 48h	92	189
Non-sterile site specimens	Blood agar, chocolate agar, CNA agar, and MacConkey agar	24h, 48h and 72h	50	109
Nasal and inguinal/perineal screening-ESwabs for MRSA and MSSA	CHROMID® MRSA (BioMérieux) and SaSelect Medium (BioRad)	18h-24h and 48h	148	181
Rectal screening-ESwabs for ESBL-producer and CPE	CHROMID® ESBL (BioMérieux) coupled to CHROMID® OXA-48 (BioMérieux)	18h-24h and 48h	84	66
		Total	483	811 / (1294 samples)

Table 7 : Definitive incubation protocoles based on the derivation and validation studies

CPE: Carbapenemase-producing *Enterobacteriaceae* , MRSA : Methicillin-resistant *Staphylococcus aureus* , MSSA: Methicillin susceptible *Staphylococcus aureus* , ESBL : Extended-spectrum beta-lactamases

Routine incubation period	Clinical samples type	WASPLab		
		Incubation time		
		Picture at T0	Intermediate incubation time	Final incubation time
18h-24h and 48h	Urine specimens	**Yes**	**18h**	**24h**
24h and 48h	Genital tract specimens	**Yes**	**16h**	**28h**
24h, 48h and 72h	Non-sterile site specimens	**Yes**	**16h**	**28h**
18h-24h and 48h	Nasal and inguinal/perineal screening-ESwabs for MRSA and MSSA	**Yes**	**No**	**18h**
18h-24h and 48h	Rectal screening-ESwabs for ESBL-producer and CPE	**Yes**	**No**	**16h**

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Automated Incubation and Digital Image Analysis of Chromogenic Media Using Copan WASPLab Enables Rapid Detection of Vancomycin-Resistant Enterococcus

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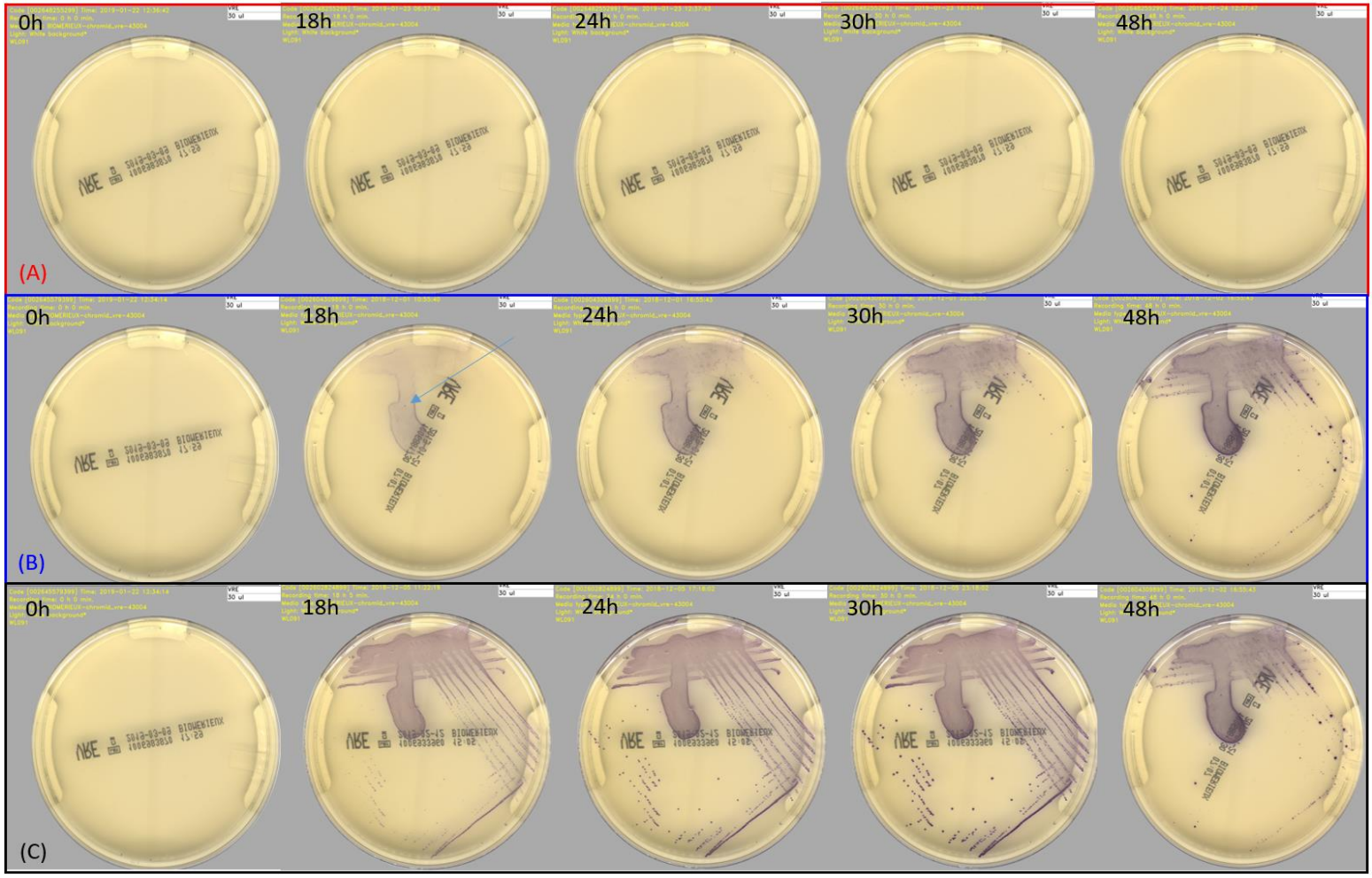


Clinical sample type	Solid culture media type	Plating volume, µl	Incubation times			
			Picture at T0	First intermediate incubation time, hr	Second intermediate incubation time, hr	Final incubation time, hr
Rectal screening-Eswab for VRE	CHROMID® VRE (BioMérieux)	30	Yes	18	24	30

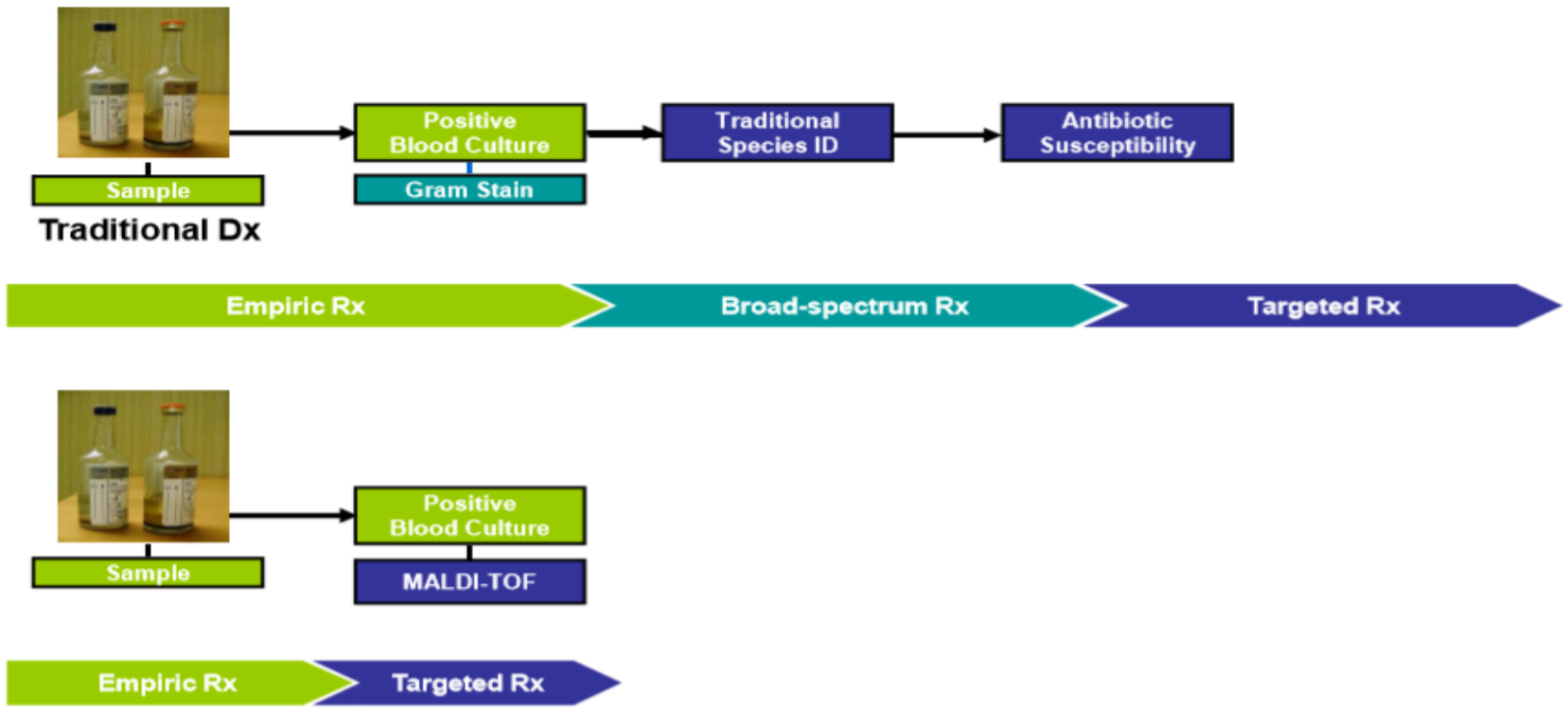
European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-020-03817-8

ORIGINAL ARTICLE

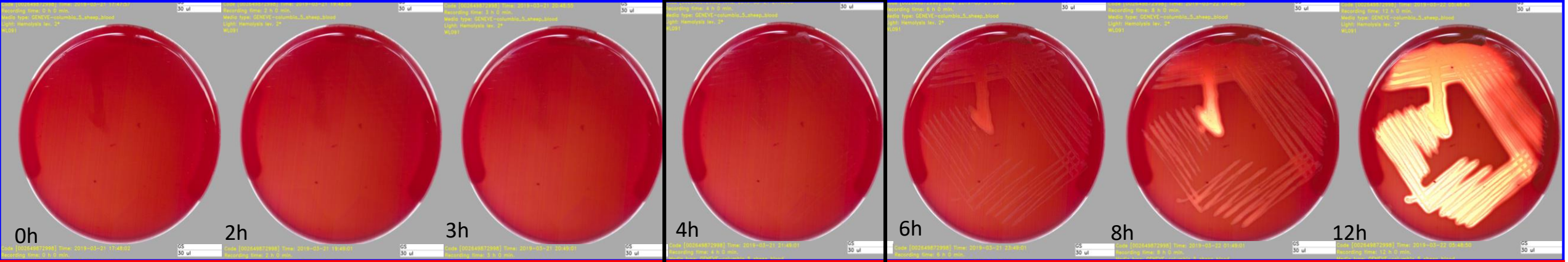
Rapid identification by MALDI-TOF/MS and antimicrobial disk diffusion susceptibility testing for positive blood cultures after a short incubation on the WASPLab

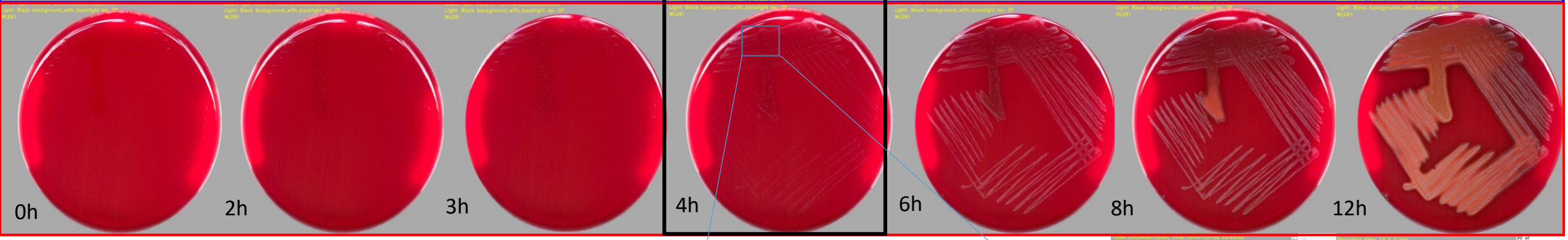
Abdessalam Cherkaoui[1] · Gesuele Renzi[1] · Nouria Azam[1] · Didier Schorderet[1] · Nicolas Vuilleumier[2,3] · Jacques Schrenzel[1,4]

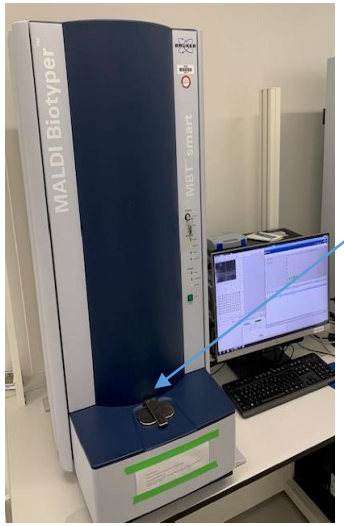
Received: 18 November 2019 / Accepted: 12 January 2020

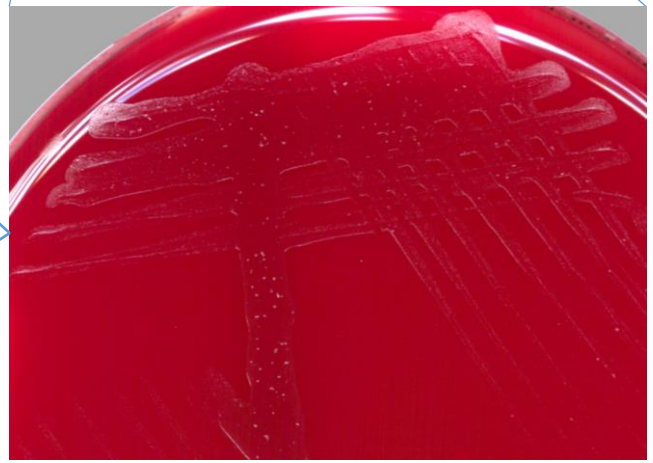


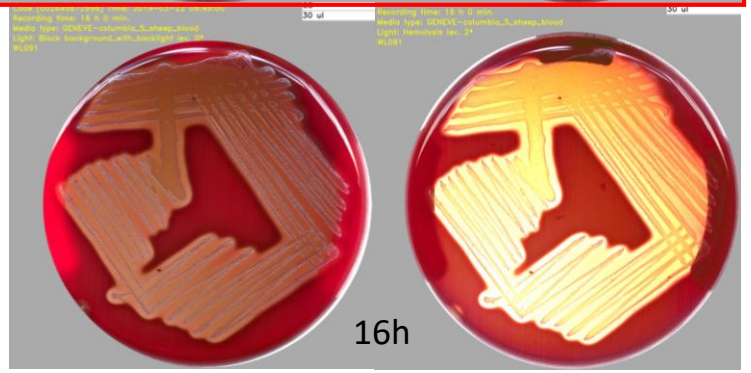
Graph adapted from AdvanDx



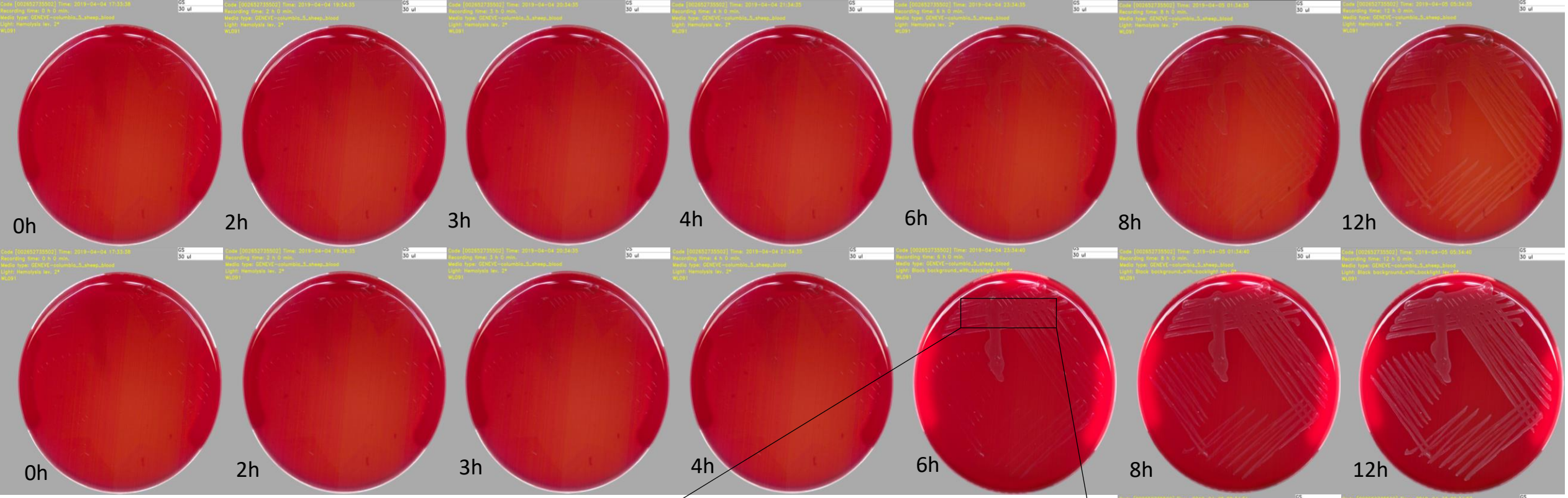


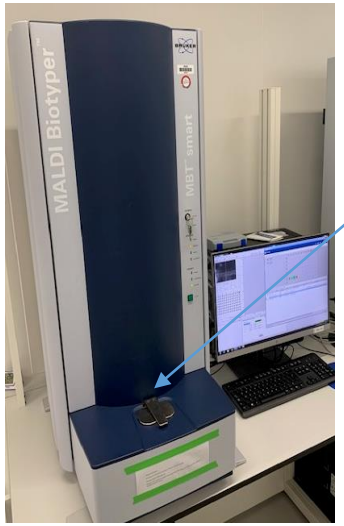


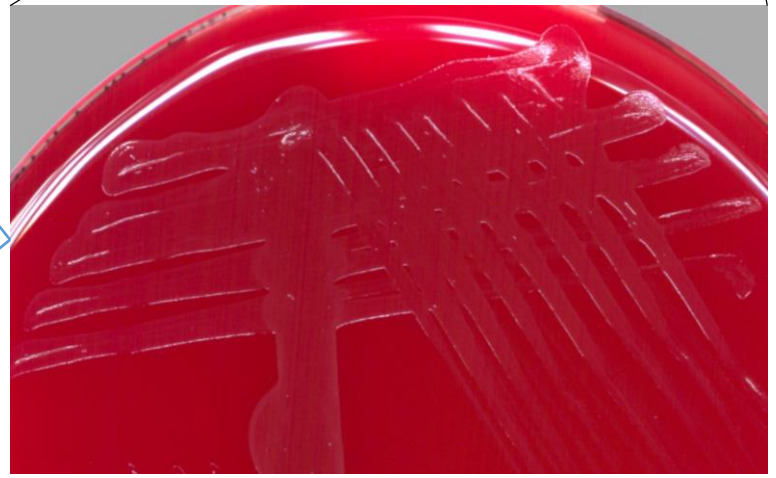




Streptococcus pyogenes







Listeria monocytogenes

Table 1 Minimal incubation times required for MALDI-TOF /MS-based species identification and AST by disk diffusion from short subcultures growing on solid media incubated on the Copan WASPLab

Microorganisms		Number of non-duplicate strains analyzed	Incubation time required for MALDITOF/MS-based species identification from short subcultures growing on solid media (hours)	Incubation time required for 0.5 McFarland suspension from short subcultures growing on solid media for AST by disk diffusion (hours)
Enterobacteriaceae	*Escherichia coli*	20	2	2
	Klebsiella pneumoniae	20	2	2
	Proteus mirabilis	20	2	2
	Salmonella	20	3	3
Non-fermenting Gram-negative bacilli	*Pseudomonas aeruginosa*	20	3	3
	Stenotrophomonas maltophilia	20	4	4
	Acinetobacter spp.	20	4	4
	Burkholderia cepacia	20	8	8
Gram-negative coccobacilli and othe Gram-negative bacilli	*Haemophilus influenzae*	20	6	6
	Pasteurella spp.	20	4	4
	Aeromonas spp.	20	3	3
Staphylococcus	*Staphylococcus aureus*	20	4	4
	Staphylococcus epidermidis	20	4	4
Streptococcus	*Streptococcus pneumoniae*	20	3	4
	Streptococcus agalactiae	20	3	4
	Streptococcus mitis	20	4	6
	Streptococcus pyogenes	20	3	4
Nutritionally deficient bacteria	*Abiotrophia*	20	6	8
	Granulicatella adiacens	20	6	8
Enterococcus	*Enterococcus faecalis*	20	3	3
	Enterococcus faecium	20	3	3
Gram-positive aerobic bacilli	*Listeria monocytogenes*	20	4	6
	Bacillus spp.	20	4	4
	Corynebacterium spp.	20	16	16
Yeast	*Candida glabrata*	20	6 (sufficent yeast biomass but no reliable identification)	
	Candida albicans	20		

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Impact of total laboratory automation on turnaround times for urine cultures and screening specimens for MRSA, ESBL, and VRE carriage: retrospective comparison with manual workflow

Abdessalam CHERKAOUI[1*], Gesuele RENZI[1], Romain MARTISCHANG[1], Stephan HARBARTH[1], Nicolas VUILLEUMIER[1], Jacques Schrenzel[1]

Impact of total laboratory automation on turnaround-time for culture-based bacteriological testing

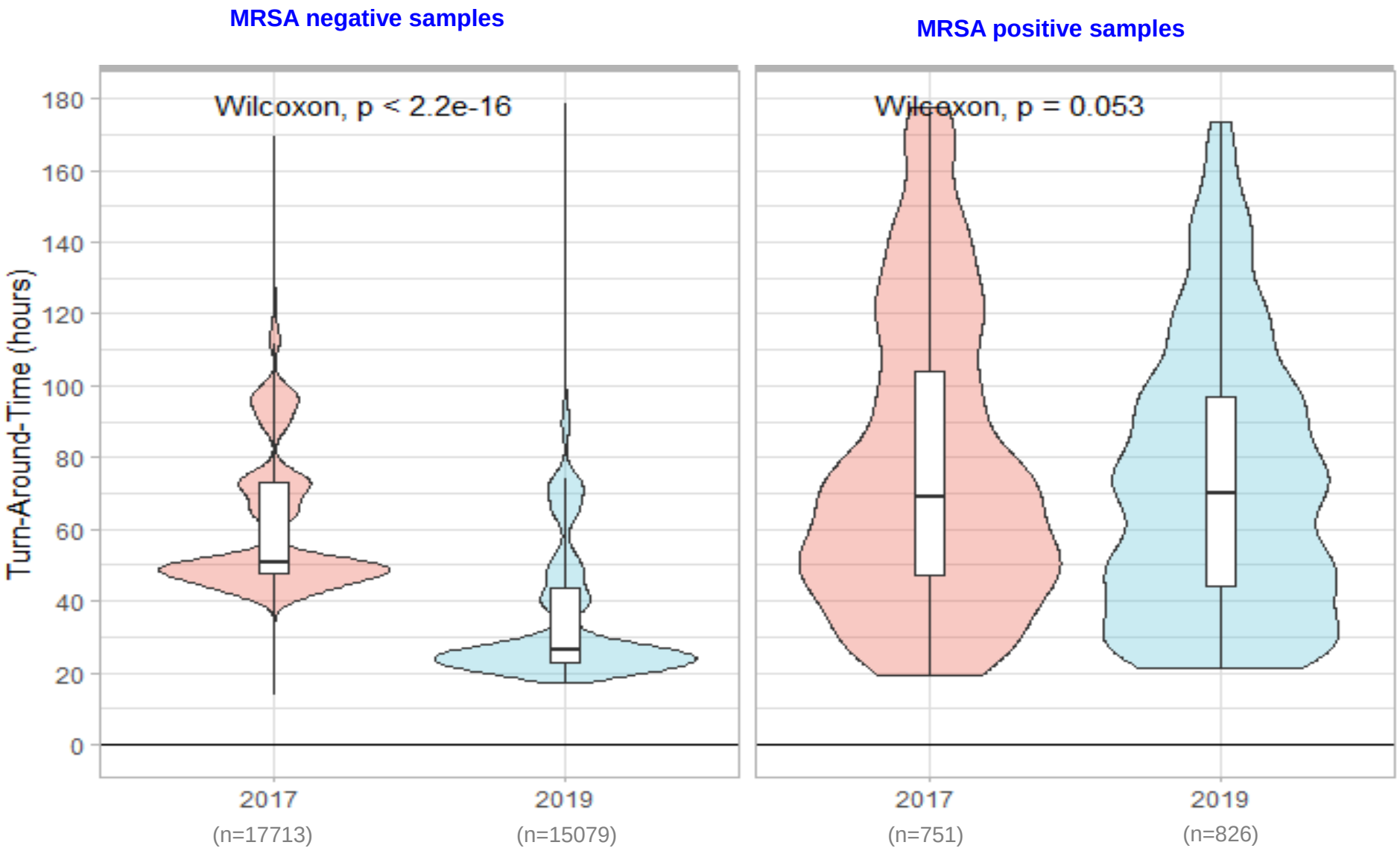
Clinical sample type	Solid culture media type	Number of samples included in this study		% of positive samples		Plating volume, µl	Time points for digital images acquisition on WASPLab				Ref.
		2017	2019	2017	2019		Picture at T0	First time point, hr	Second time point, hr	Final time point, hr	
Urine specimens	CHROMID® CPS® Elite (BioMérieux)	19937	18226	**51%** (10080/19937)	**51%** (9343/18226)	10	Yes	18	No	24	[1]
Nasal and inguinal/perineal screening-Eswab for MRSA	CHROMID® MRSA (BioMérieux)	18464	15905	**4%** (751/18464)	**5%** (826/15905)	30	Yes	No	No	18	[1]
Rectal screening-Eswab for ESBL	CHROMID® ESBL (BioMérieux)	7803	8643	**27%** (2140/7803)	**25%** (2198/8643)	30	Yes	No	No	16	[1]
Rectal screening-Eswab for VRE	CHROMID® VRE (bioMérieux)	1973	7464	**2%** (45/1973)	**0.8%** (58/7464)	30	Yes	18	24	30	[2]

Table 1 Workup of bacterial culture, samples included in this study, and analysis parameters on the WASPLab based on previous studies.

1) Cherkaoui et al. Clinical Microbiology and Infection April 2019

2) Cherkaoui et al. Frontiers in Cellular and Infection Microbiology Nov. 2019

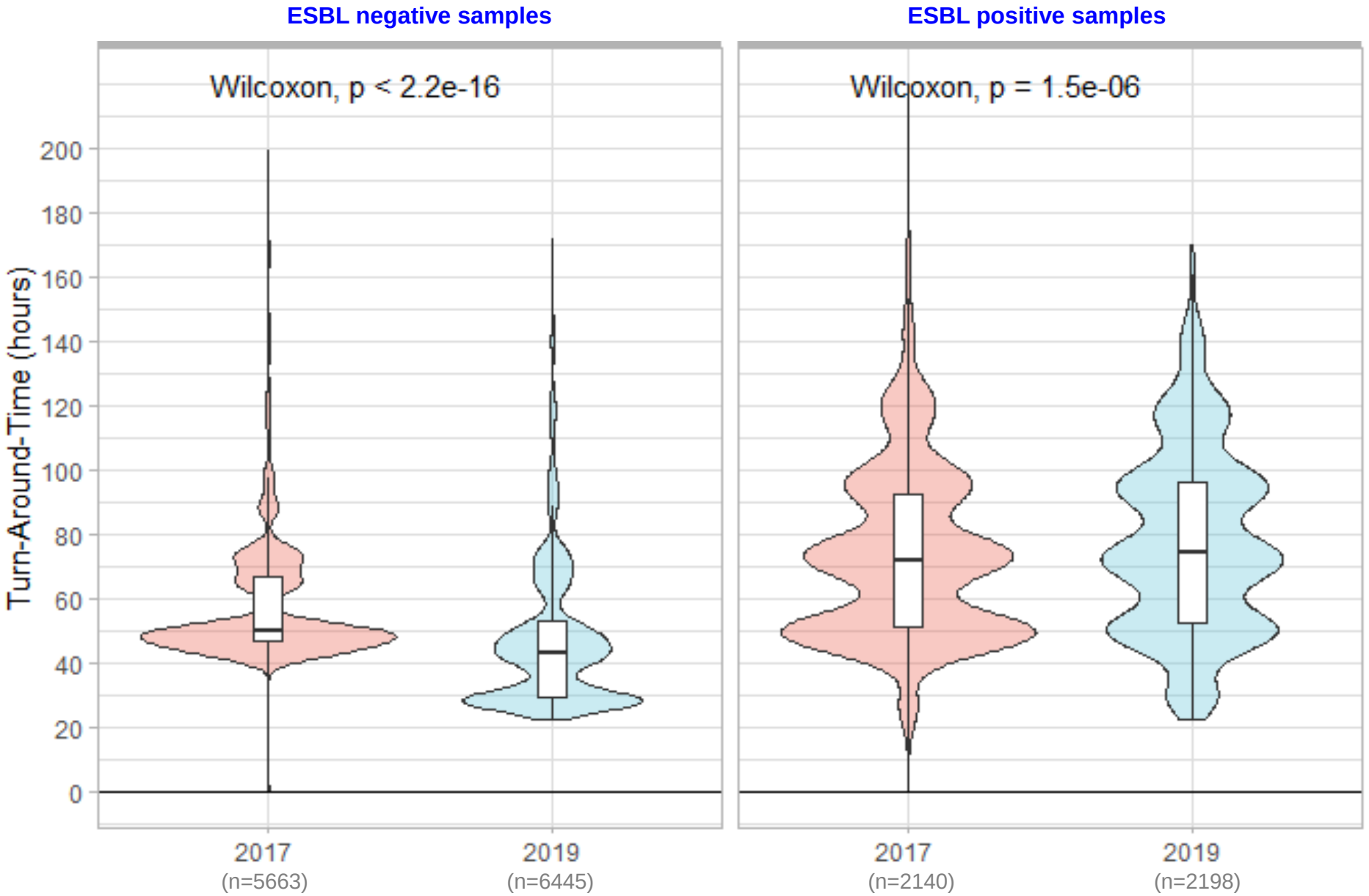
Turnaround time (from reception of samples to when the result is released to the ordering provider) for nasal and inguinal/perineal screening-ESwab for methicillin-resistant *Staphylococcus aureus* (**MRSA**) by culture



MRSA		Median TAT (hr)
Negative	2017	**50.4**
samples	2019	**25.8**
Positive	2017	70.1
samples	2019	70.3

Cherkaoui et al. 2020 / Frontiers in Cellular and Infection Microbiology

Turnaround time (from reception of samples to when the result is released to the ordering provider) for rectal screening-ESwab for extended-spectrum beta-lactamases (**ESBLs**) by culture



ESBL		Median TAT (hr)
Negative samples	2017	**49.8**
	2019	**42**
Positive samples	2017	68
	2019	73.4

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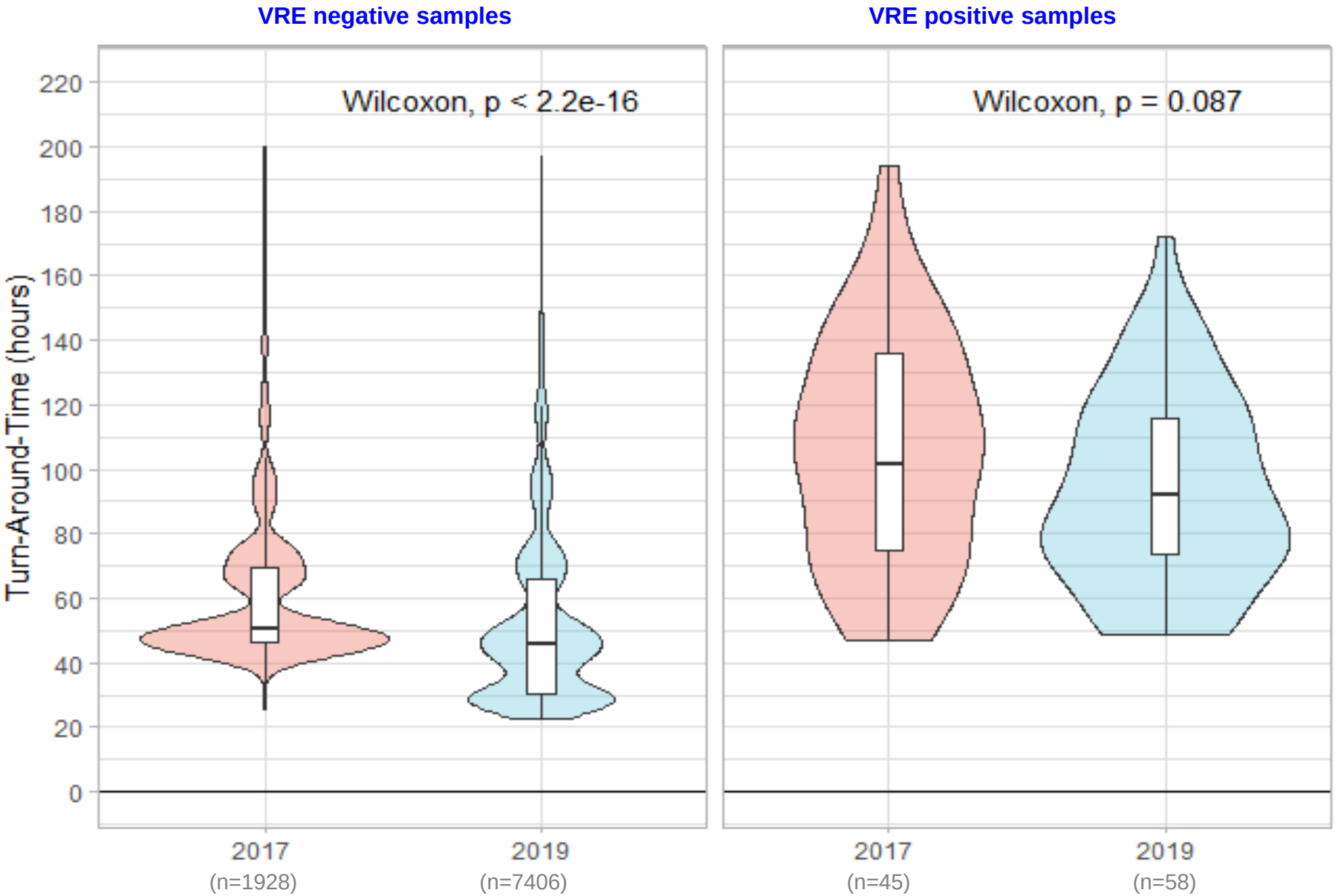
Turnaround time (from reception of samples to when the result is released to the ordering provider) for rectal screening-ESwab for vancomycin-resistant *Enterococcus* (**VRE**) by culture



VRE		Median TAT (hr)
Negative samples	2017	**50.6**
	2019	**45.7**
Positive samples	2017	**102**
	2019	**92.2**

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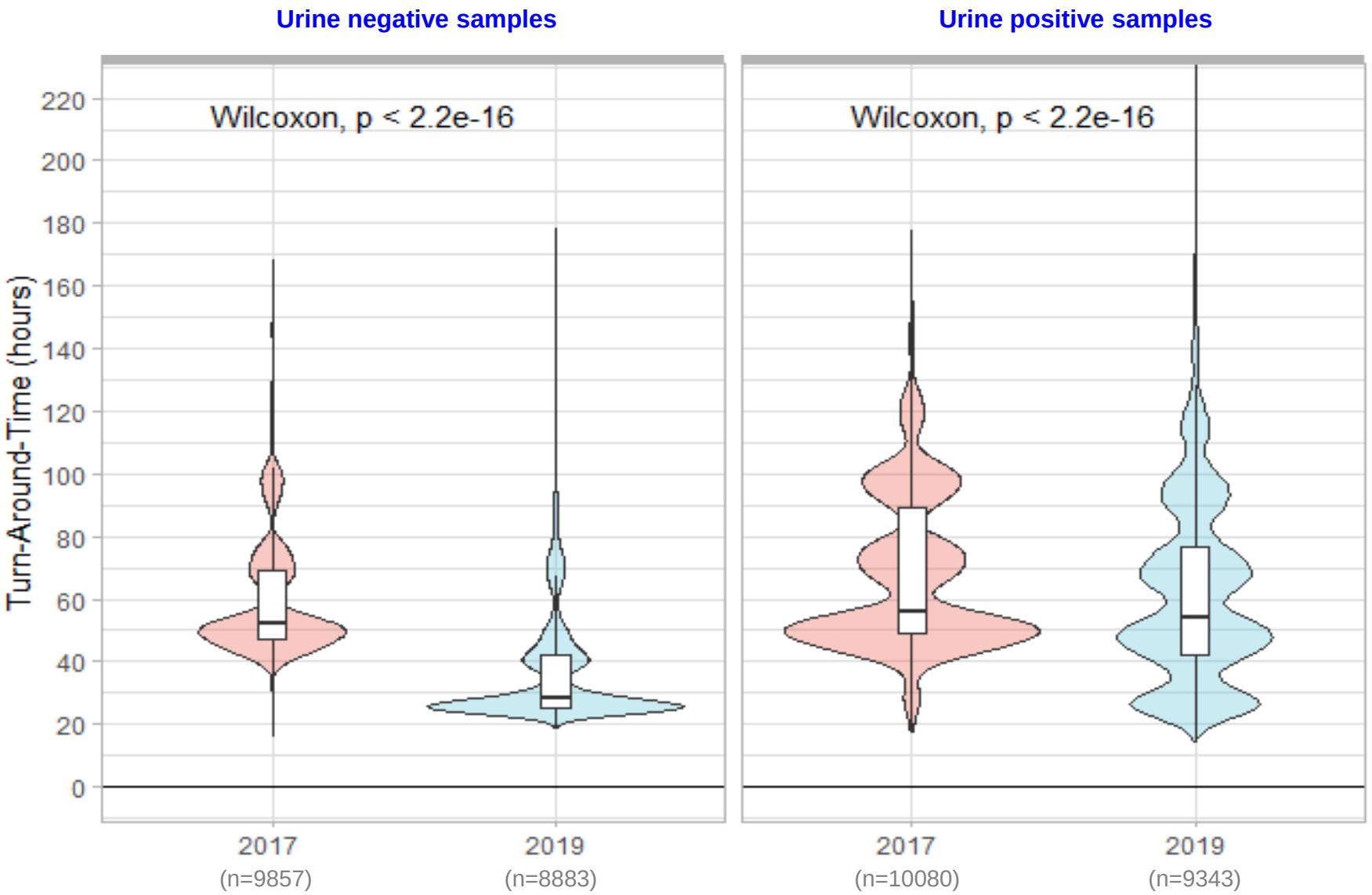
Turnaround time (from reception of sample to when the result is released to the ordering provider) for a **urine culture**



Urine		Median TAT (hr)
Negative samples	2017	**51.3**
	2019	**27.3**
Positive samples	2017	**54.8**
	2019	**52.5**

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TABLE 2 | Turnaround-times (from reception of samples to delivery of the culture results).

	Year	Urine cultures (h)		Screening for MRSA carriage (h)		Screening for ESBL carriage (h)		Screening for VRE carriage (h)	
Negative samples	2017	52.1	$P < 0.001$	50.7	$P < 0.001$	50.2	$P < 0.001$	50.6	$P < 0.001$
	2019	28.3		26.3		43.0		45.7	
Positive samples	2017	56.2	$P < 0.001$	69.2	$P = 0.053$	72.0	$P < 0.001$	102.0	$P = 0.087$
	2019	54.0		70.2		74.4		92.2	

Fully Automated solution for Antimicrobial Disk Diffusion Susceptibility Testing

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

BACTERIOLOGY

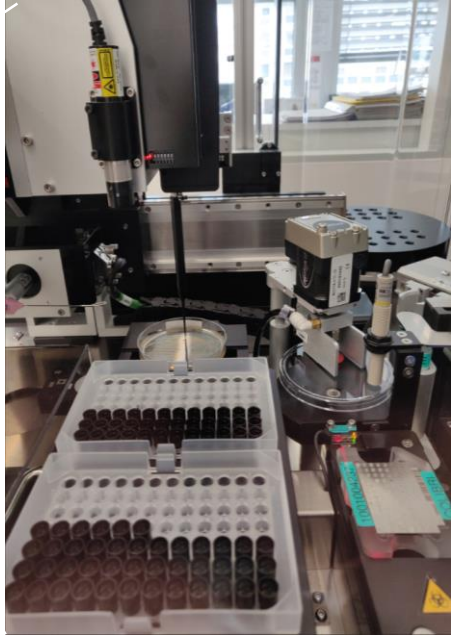
Performance of Fully Automated Antimicrobial Disk Diffusion Susceptibility Testing Using Copan WASP Colibri Coupled to the Radian In-Line Carousel and Expert System

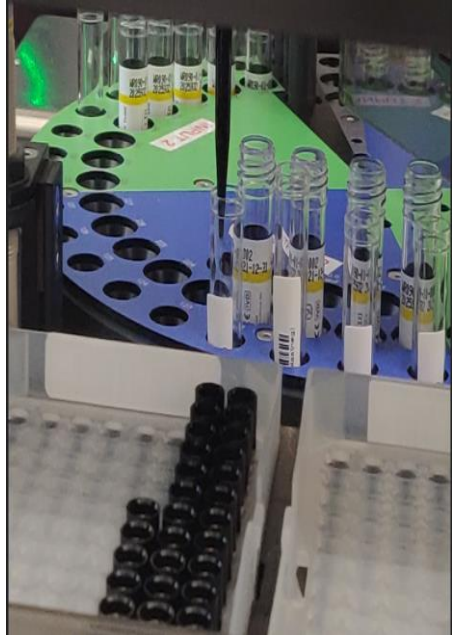
Abdessalam Cherkaoui,[a] Gesuele Renzi,[a] Nicolas Vuilleumier,[b] Jacques Schrenzel[a,c]

[a]Bacteriology Laboratory, Division of Laboratory Medicine, Department of Diagnostics, Geneva University Hospitals, Geneva, Switzerland
[b]Division of Laboratory Medicine, Department of Diagnostics, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland
[c]Genomic Research Laboratory, Division of Infectious Diseases, Department of Medicine, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

September 2021 Volume 59 Issue 9 e00777-21

Versus



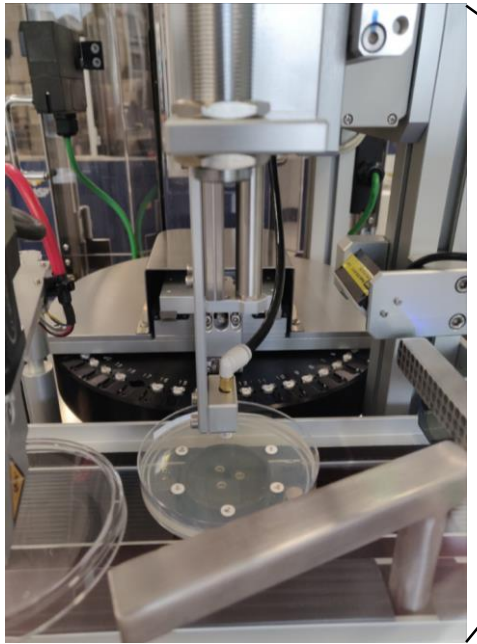


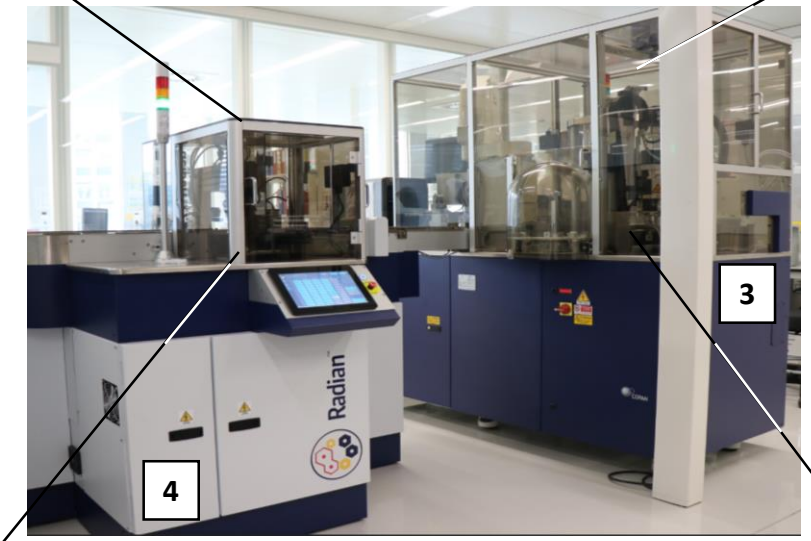
2) Colibri™
The AST inoculum is prepared in strict accordance with the manufacturer's instructions

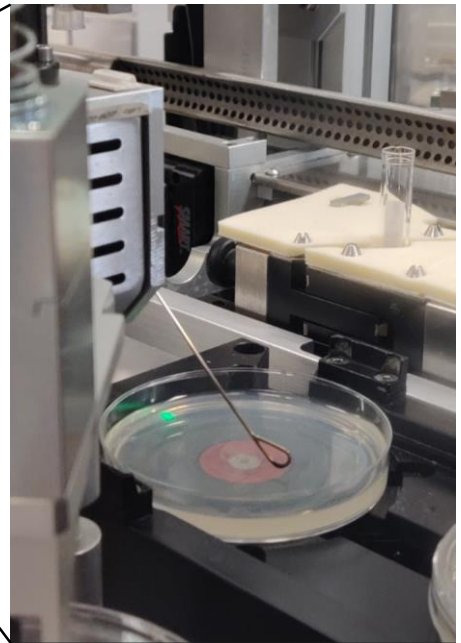
1) WASPLab® : digital plate images
To capture the relevant heterogeneity profiles for the same strain, the minimum number of pickpoints required by the system to prepare the AST inoculum is defined as follows :

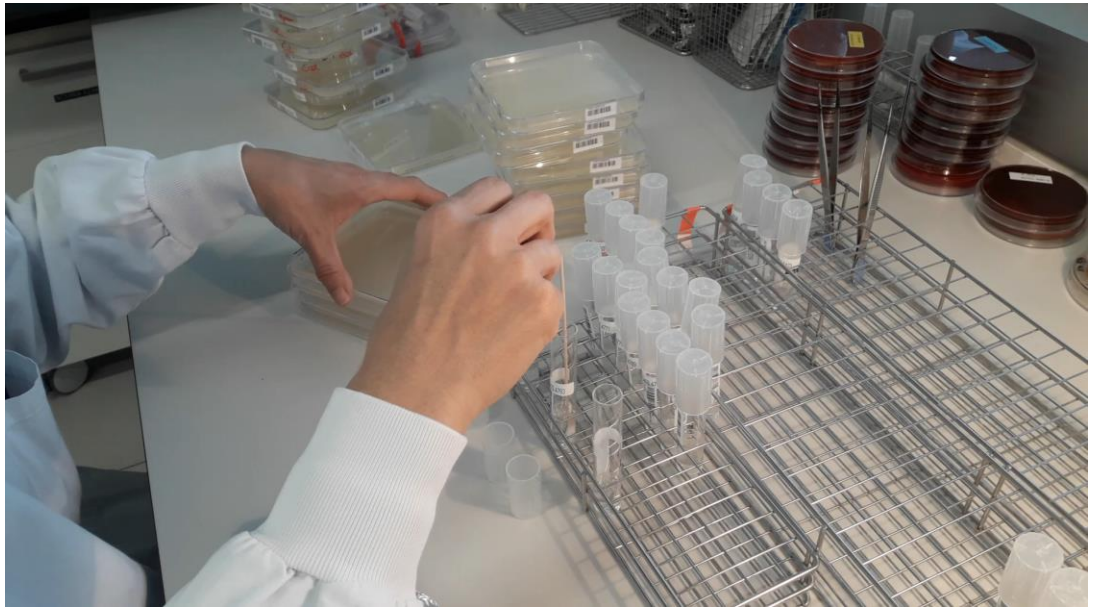
- Six different pickpoints for Gram positive bacteria
- Four different pickpoints for Gram negative bacteria

3) WASP™ : The AST inoculum (2x30 µl loop/spreader) is spread over the entire surface of the round Mueller-Hinton agar plate according to the defined AST streaking pattern
4) Radian™ in Line Carousel: distributes the antibiotic discs

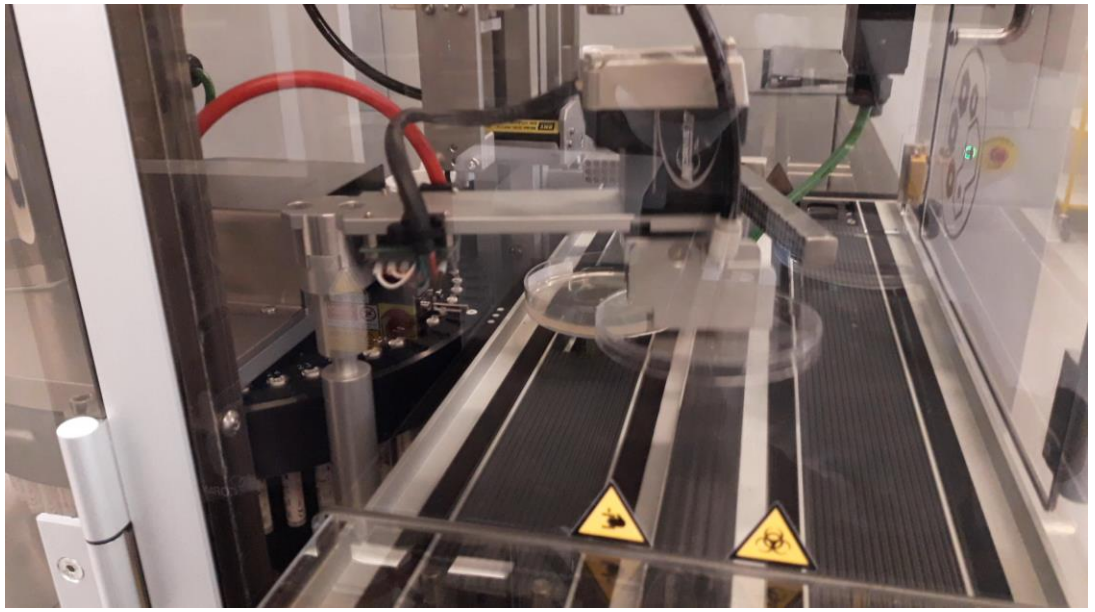




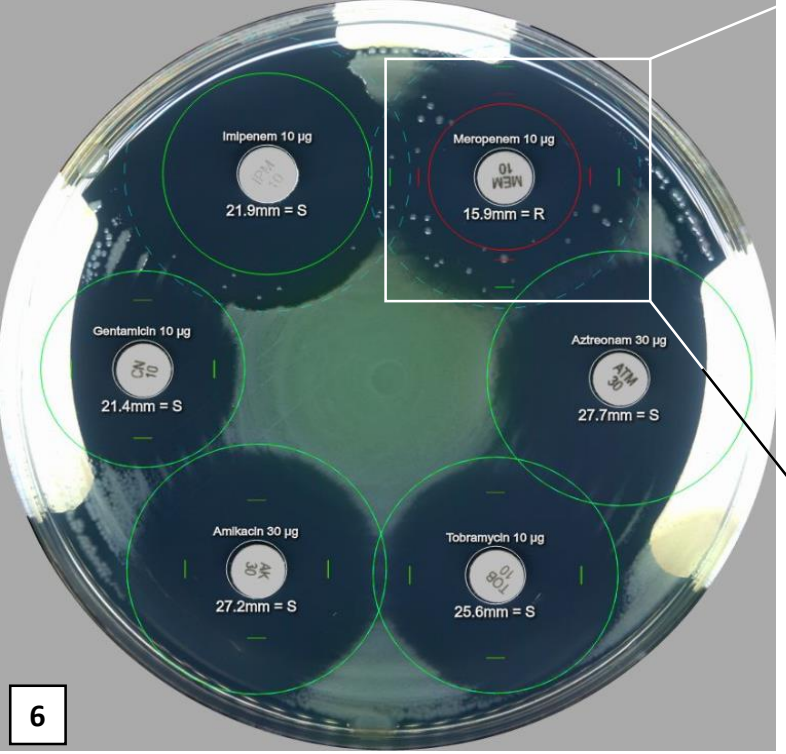




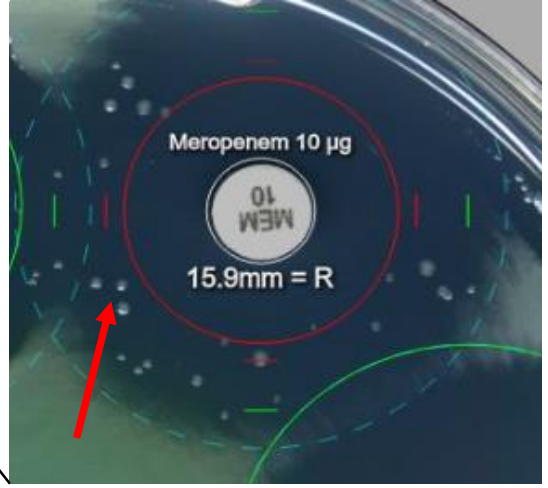
Traditional Manual Process



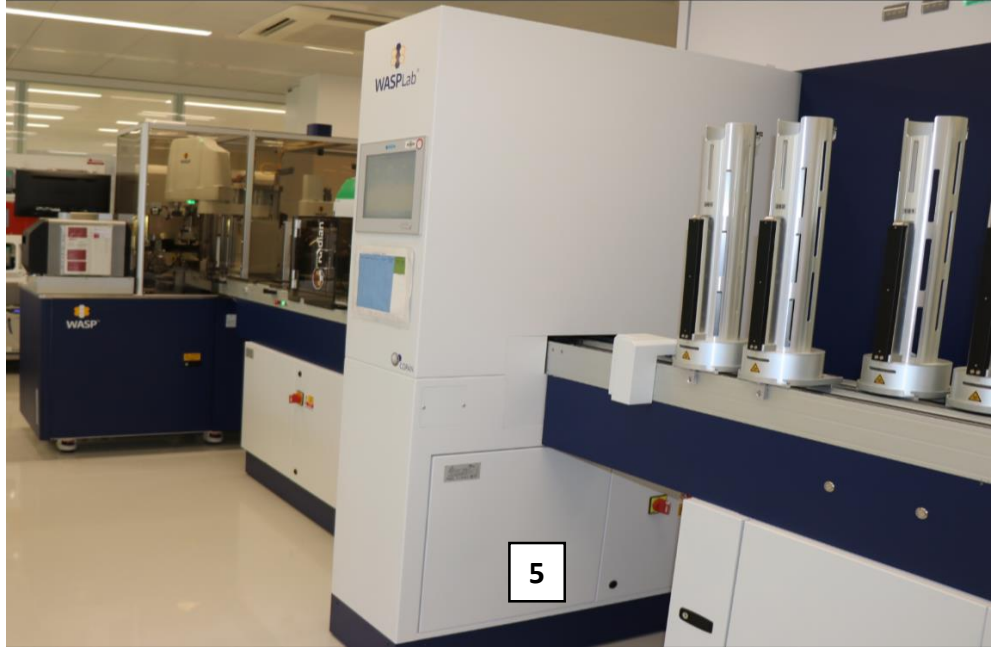
Fully Automated Process



6) Radian™ Expert System: Automatic reading of the inhibition zone diameters and AST interpretation for *Pseudomonas aeruginosa* strain



Heteroresistant populations (colonies visible within the inhibition halo, red arrow)



5) WASPLab® AST Line :
AST plates are digitized after 16 hours of incubation

Figure-1 (Parts 1 to 6): Workflow of a fully automated solution for antimicrobial disk diffusion susceptibility testing (Colibri™, WASP™, Radian™ in-Line Carousel, and Radian™ Expert System)
Colibri™ prepares the inocula for 10 strains within 21 min
AST Line (WASP™ + Radian™ in Line Carousel) executes AST for 10 strains (i.e. 40 media plates and 200 antibiotic discs) within 44 min

Antibiotics	Resistance rate % (no. of isolates)	Categorical agreement between the compared methods (%)	Colibri™ coupled to Radian™		VITEK 2® system	
			Very major error	Major error	Very major error	Major error
Enterobacterales species (n=292)						
Ampicillin	66 (193)	100				
Amoxicillin/Clavulanate	37 (108)	99.7		1		
Piperacillin/Tazobactam	21 (62)	98.6		2	2	
Cefuroxime	25 (73)	100				
Ceftazidime	22 (63)	99.3		2		
Ceftriaxone	22 (63)	99.3		2		
Cefepime	19 (56)	99		1	3	
Imipenem	6 (18)	98.6		2	1	1
Meropenem	7 (19)	99.7			1	
Ertapenem	17 (49)	97.6		3	4	
Amikacin	7 (19)	99.7			1	
Gentamicin	15 (45)	99.7		1		
Norfloxacin	35 (101)	100				
Ciprofloxacin	29 (85)	99.3				2
Co-trimoxazole	35 (103)	99.7		1		
Pseudomonas aeruginosa **(n=198)**						
Piperacillin	43 (85)	94	1		11 (incl. 5*)	
Piperacillin/Tazobactam	33 (65)	98.5			1	2
Ceftazidime	28 (56)	99.5		1		
Cefepime	28 (55)	99		1	1*	
Imipenem	30 (60)	98.5	1		2*	
Meropenem	27 (53)	98			4*	
Amikacin	24 (47)	99.5				1
Gentamicin	21 (42)	99				2
Tobramycin	23 (46)	100				
Ciprofloxacin	25 (49)	99.5				1
Levofloxacin	31 (61)	99			2 (incl. 1*)	

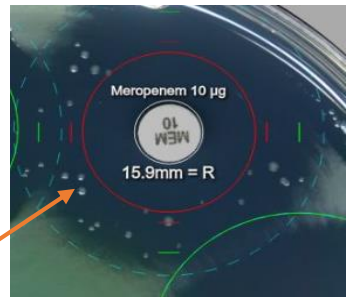
*Presence of colonies within the inhibition halo (heteroresistance detected only by disk diffusion)

The overall categorical agreements between the two compared methods

99.3% (4350/4380; 95% CI 99% to 99.5%)

98.6% (2147/2178; 95% CI 98.0% to 99.0%)

The most important cause of the very major errors encountered on the Vitek 2 for *P. aeruginosa* (62%, 13/21) was related to the presence of **heteroresistant populations**



Antibiotics	Resistance rate % (no. of isolates)	Categorical agreement between the compared methods (%)	Colibri™ coupled to Radian™		VITEK 2® system	
			Very major error	Major error	Very major error	Major error
Staphylococcus **spp. (n=185 including 107 *Staphylococcus aureus* and 78 Coagulase-negative staphylococci)**						
Cefoxitine	32 (60)	100				
Gentamicin	21 (39)	100				
Ciprofloxacin	32 (60)	99.5			1	
Clindamycin	29 (53)	100				
Erythromycin	34 (62)	100				
Fusidic acid	26 (48)	100				
Co-trimoxazole	23 (42)	94.6			10	
Rifampicin	3 (6)	100				
Tigecyclin	0	100				
Linezolid	0	100				
Enterococcus spp. (n=43 including 38 *Enterococcus faecalis* and 5 *Enterococcus faecium*)						
Ampicillin	9 (4)	97.7		1		
Imipenem	9 (4)	97.7			1	
Gentamicin	9* (4)	100				
Linezolid	0	100				
Teicoplanin	0	100				
Vancomycin	0	100				
Tigecycline	0	100				
Nitrofurantoin	0**	100				

*High level of gentamicin resistance / **only *Enterococcus faecalis* isolates were included

The overall categorical agreements between the two compared methods

99.4% (1,839/1,850; 95% CI 98.9% to 99.7%)

These very major errors were reported only for coagulase-negative staphylococci (one *S. hominis* and nine *S. epidermidis*)
No strictly explication has been found

99.4% (342/344; 95% CI 97.9% to 99.8%)

Isolates tested (no. of strains)	Colibri coupled to Radian AST line		VITEK 2 system	
	Cost (EUR)		Cost (EUR)	
	Avg per isolate	Total	Avg per isolate	Total
Enterobacterales (292)	4.6	1343.2	8	2336
Pseudomonas aeruginosa (198)	3.18	629.6	8	1584
Staphylococcus spp. (185)	3.05	564.3	8	1480
Enterococcus spp. (43)	2.79	120	8	344
Total		**2657.1**		**5744**

Table-3 : Consumable costs estimate of the AST performed by the two compared methods

For AST by Colibri coupled to Radian AST line, we included only the costs of the media plates and of the specific panel of antibiotic discs tested
For the AST by VITEK 2, we included only the costs of the AST cards

Conclusions

The Colibri coupled to the Radian provide a fully automated solution for AST by disk diffusion with an accuracy that is equal to or better than that of the Vitek 2 system.

By implementing the full automation of AST process in a stepwise manner (IT development, validation of the performances, staff training, and then routine implementation) we have become able to reach **97% (95 to 110 AST panels per day / 270 to 300 plates)** of our routine AST panels performed by **the Colibri coupled to the Radian within 5 months.**

TABLE 3 Hallmarks of the phenotypic AST methods compared in this study

Colibri coupled to Radian	VITEK 2 system
Fully automated method	Semiautomated method
Easy to change the antibiotics tested	
Greatest flexibility and cost-effectiveness	Less flexible and more expensive (susceptibility cards)
Reliable for detecting heteroresistant subpopulations	Low sensitivity for the detection of heteroresistant subpopulations
Easy to see test failures (e.g., mixed inoculum)	Purity check plates are mandatory (more consumable and additional workload)
More accurate detection of new resistance mechanisms	Problems in detecting some patterns of carbapenemases (e.g., OXA-48-like producers)
Applicable to many fastidious organisms	The range of drug dilution is usually very narrow
Inability to provide precise data regarding the level of an organism's resistance or susceptibility	Provides a good approximation of the MIC

Impact clinique de l'automation…

- Valeur médicale
  - Réduire les temps de rendu de résultats médicalement actionnables
    - Détection / exclusion de pathogènes MDRO
    - Identification rapide des pathogènes
    - Antibiogrammes rapides

Merci pour votre attention