



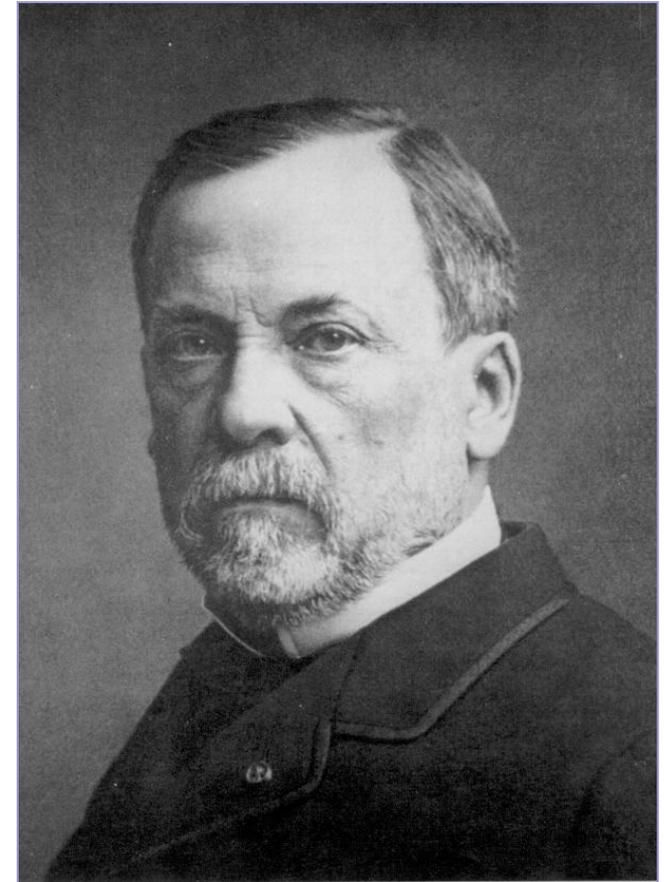
(Semi)-automated reading of inhibition zones

Pr Jacques Schrenzel, MD

Head of the Bacteriology Laboratory (LB)
and of the Genomic Research Laboratory (GRL)

Service of Infectious Diseases, HUG, Geneva

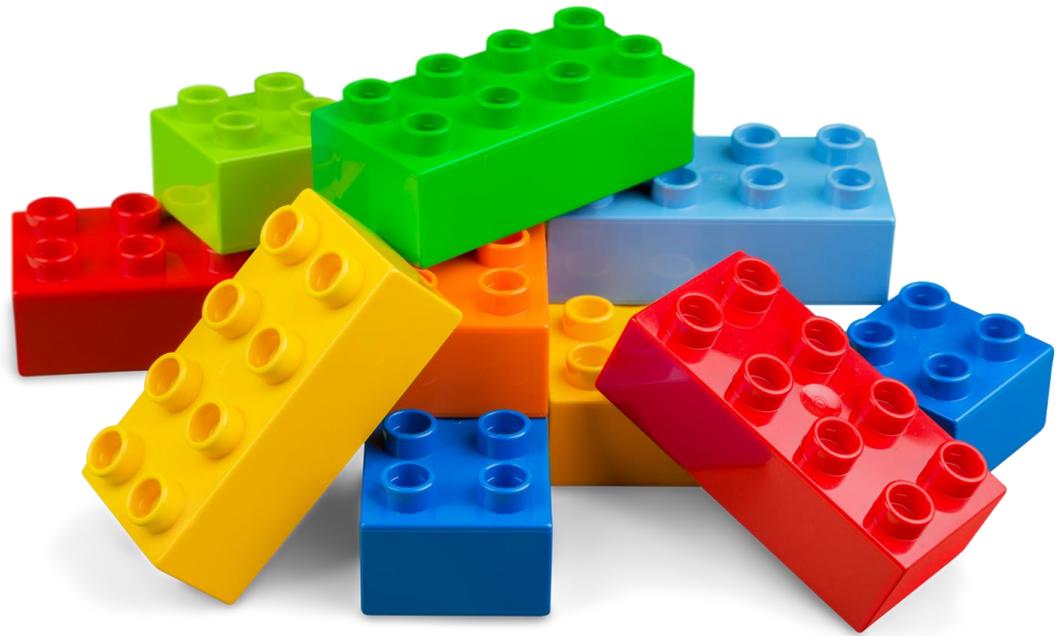
Thinking of microbiology ?



Louis Pasteur (1822-1895)



Objectives ?





Objectives ?

Benefit patients

Ensure highest results quality

Reduce TAT

Enable more analyses

Develop post-analytical skills

=> Patients outcomes

Transform the laboratory

Standardization and documentation of lab processes. Education of personnel

Full automation

Reorganization of lab workflows

Enable digitalization and implement AI

=> Lab efficiency and costs

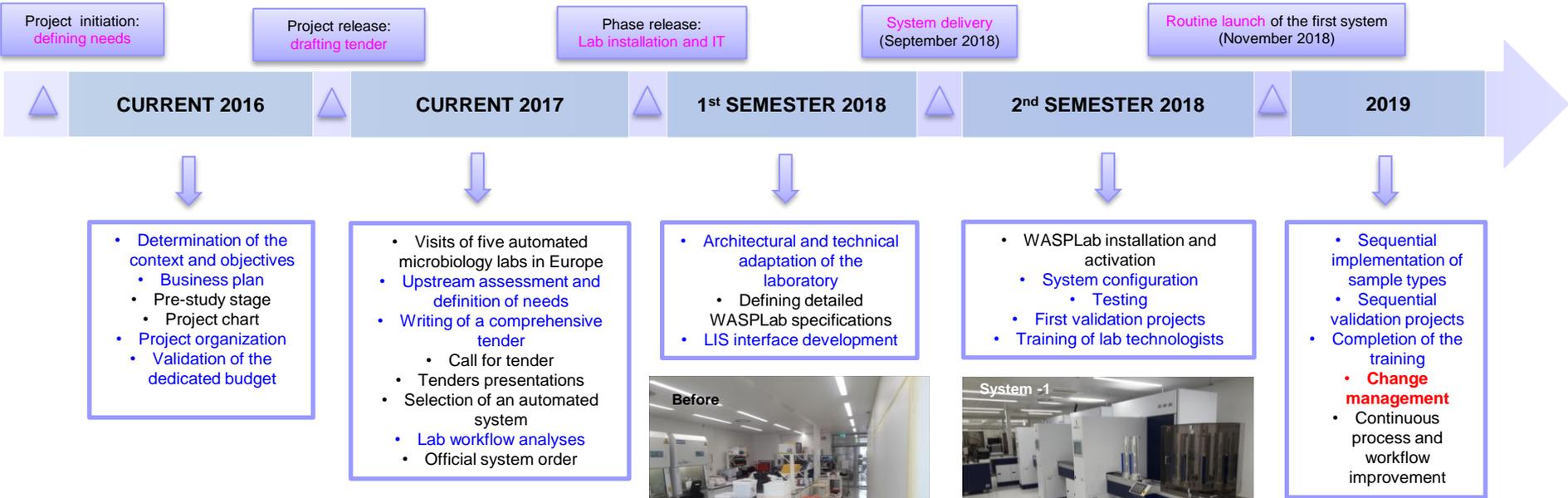


21.09.2018

Implementation



28.09.2018



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

System-2 for AST is composed of 1 WASP, and 1/2 “air atmosphere” incubator.

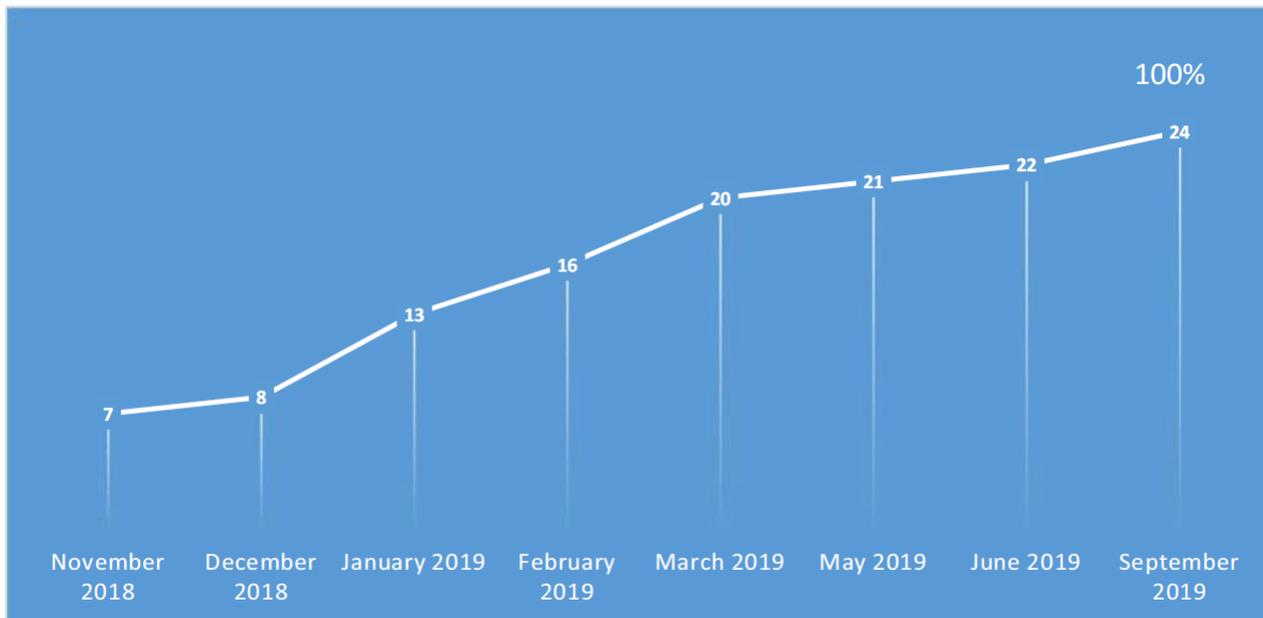
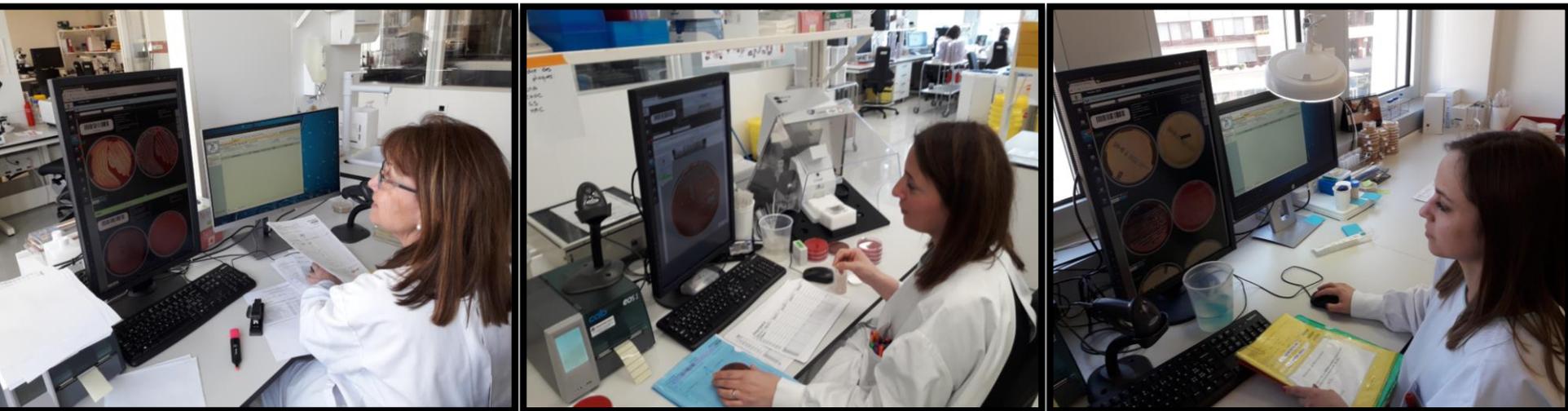
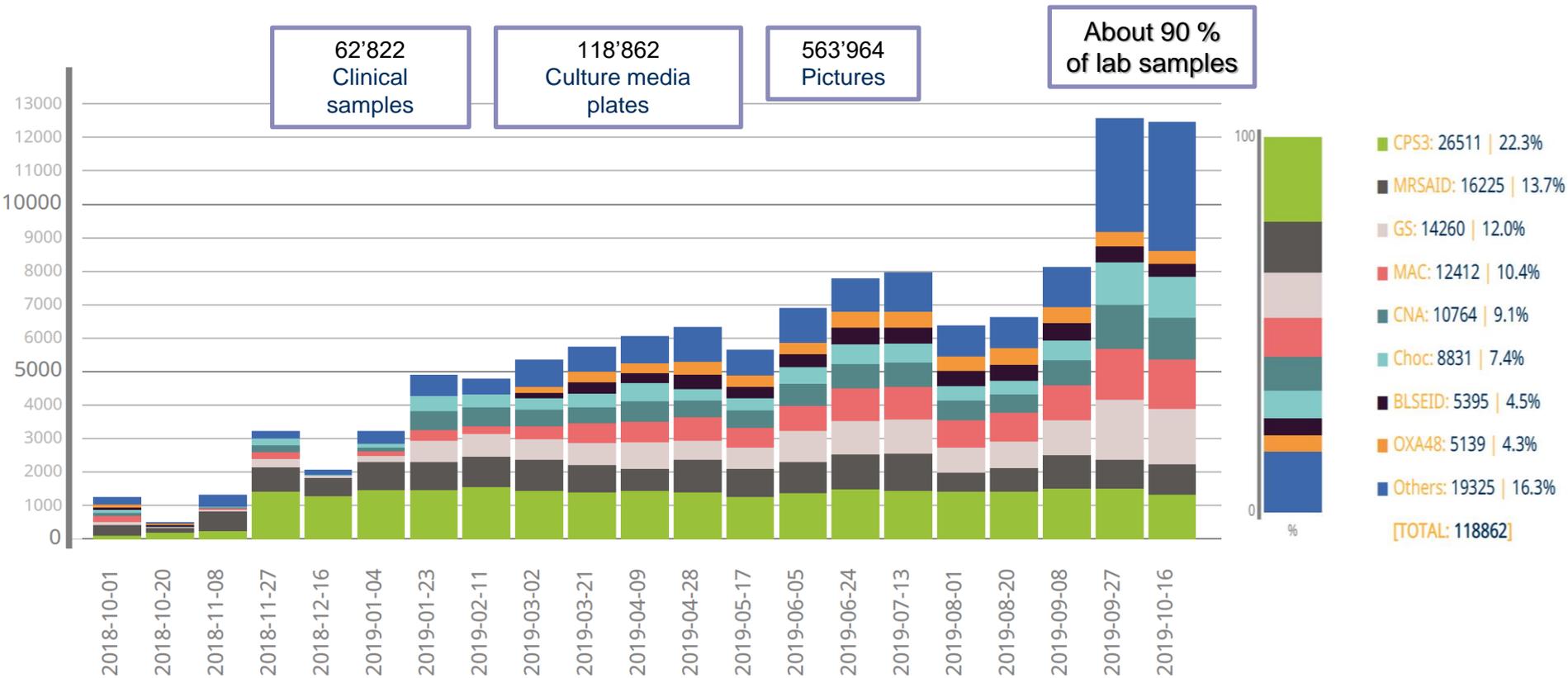


Fig. 2 Number of laboratory technologists trained to perform bacteriology analyses on the WASPLabTM



Sequential implementation of the various sample types (Oct 2018 - Oct 2019)



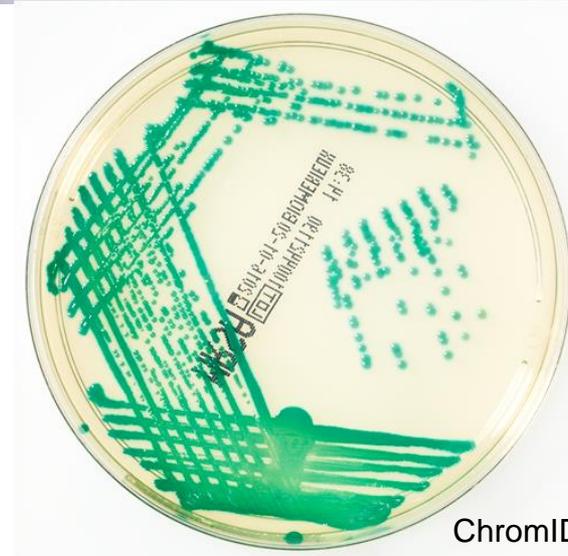
(Cherkaoui A. et al, Eur J Clin Microbiol Infect. 2020 PMID: **32248509**)

(Cherkaoui A. et al, Clin Microbiol Infect. 2019 PMID: **30986560**)

(Cherkaoui A. et al, Clin Microbiol Infect. 2019 PMID: **31733376**)

(Cherkaoui A. et al, Front Cell Infect Microbiol. 2019 PMID: **31781516**)

Detecting MRSA

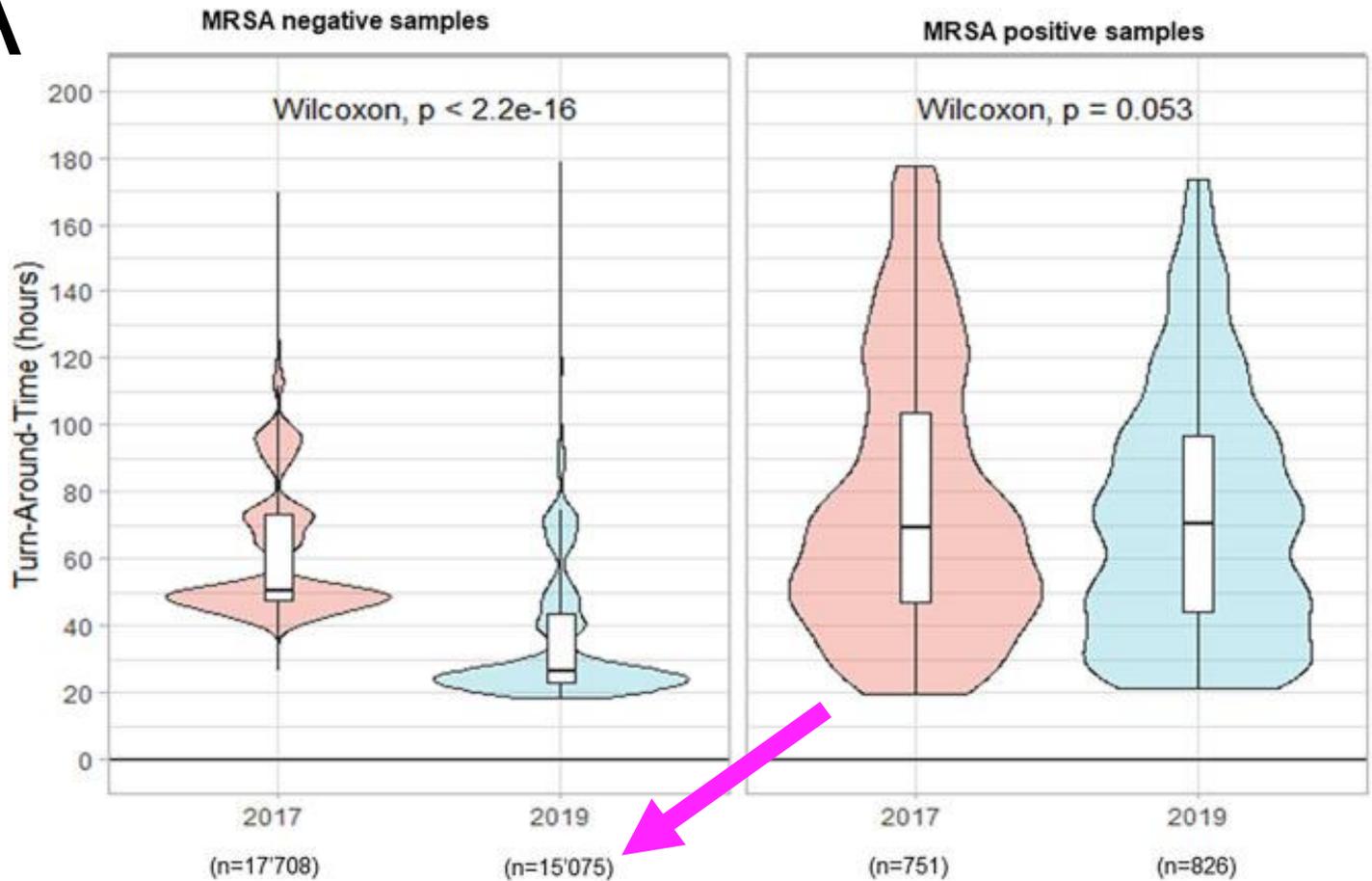


ChromID™ MRSA

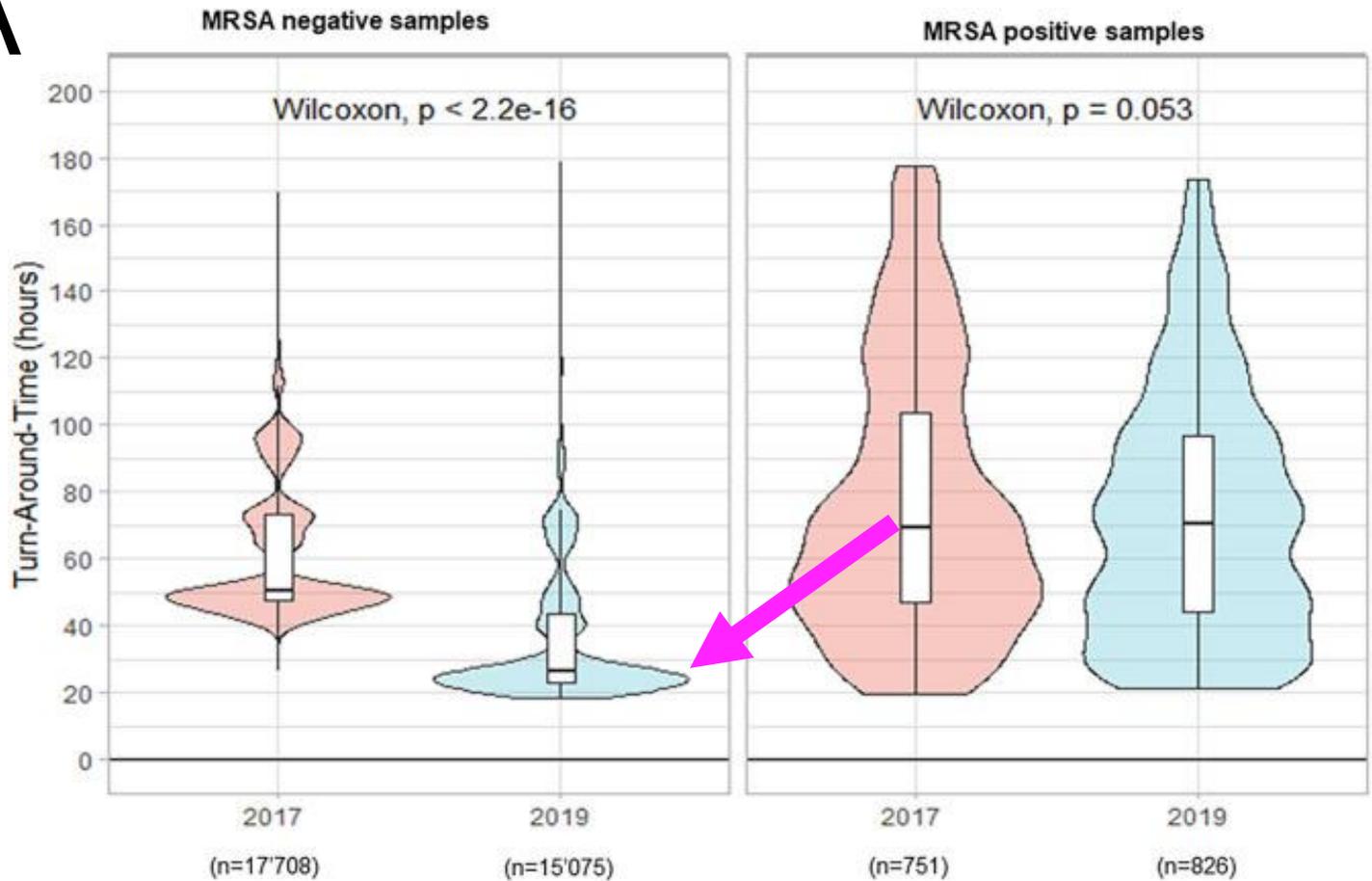
WASPLab detection of MRSA:
100% at 18h

training set: 483 samples
validation set: 811 samples

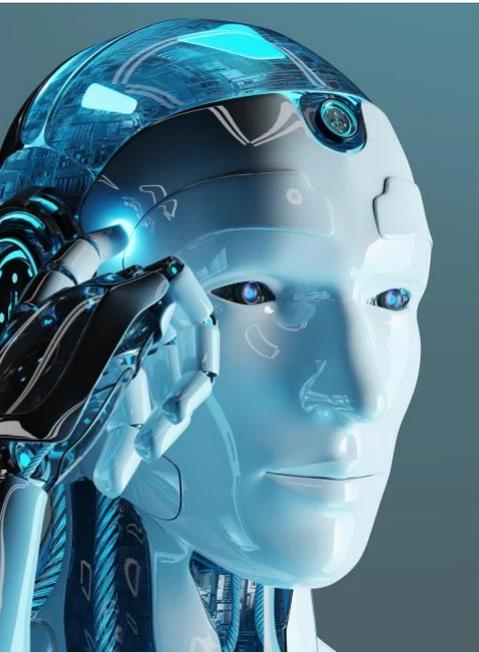
MRSA



MRSA



Phenomatrix

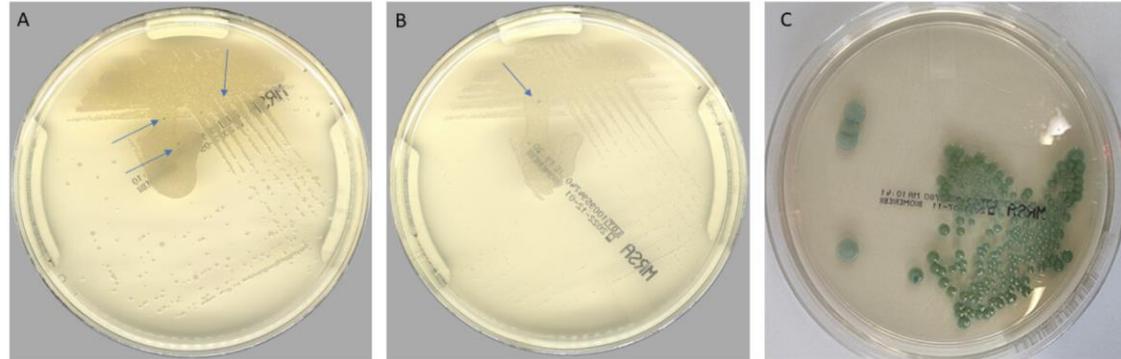
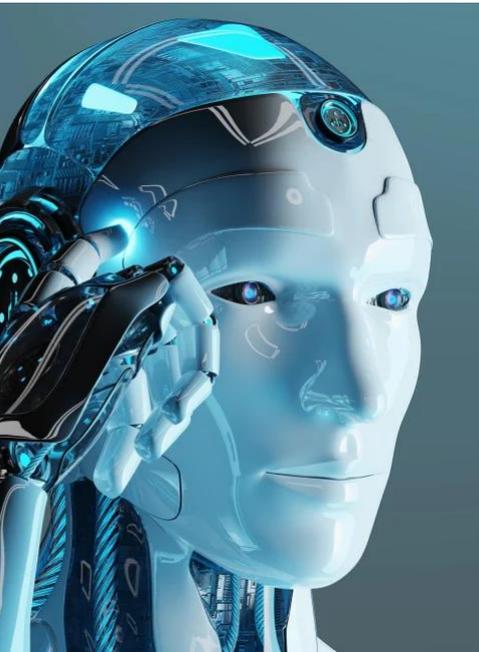


		Manuel work-up		
		NEG	POS	Total
Phenomatrix	NEG	16'209	2	16'211
	POS	146	866	1'012
	Total	16'355	868	17'223

(Cherkaoui A. et al, Clin Microbiol Infect 2019, PMID: **30986560**)

(Cherkaoui A. et al, J Clin Microbiol 2024, PMID: **38126761**)

Phenomatrix



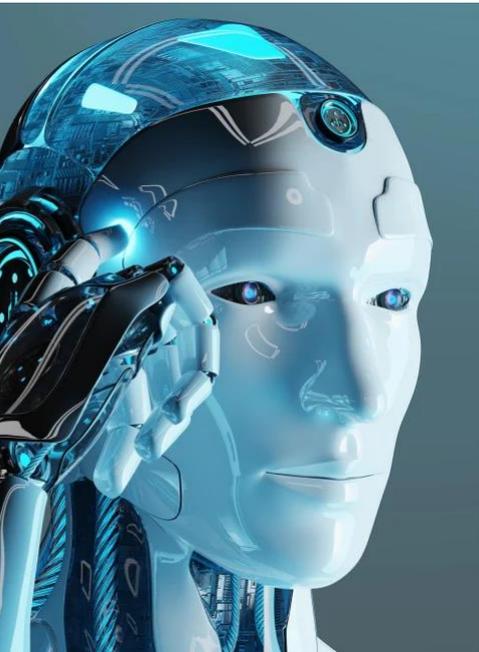
		Manuel work-up		
		NEG	POS	Total
Phenomatrix	NEG	16'209	2	16'211
	POS	146	866	1'012
	Total	16'355	868	17'223

(Cherkaoui A. et al, Clin Microbiol Infect 2019, PMID: 30986560)

(Cherkaoui A. et al, J Clin Microbiol 2024, PMID: 38126761)

Phenomatrix +

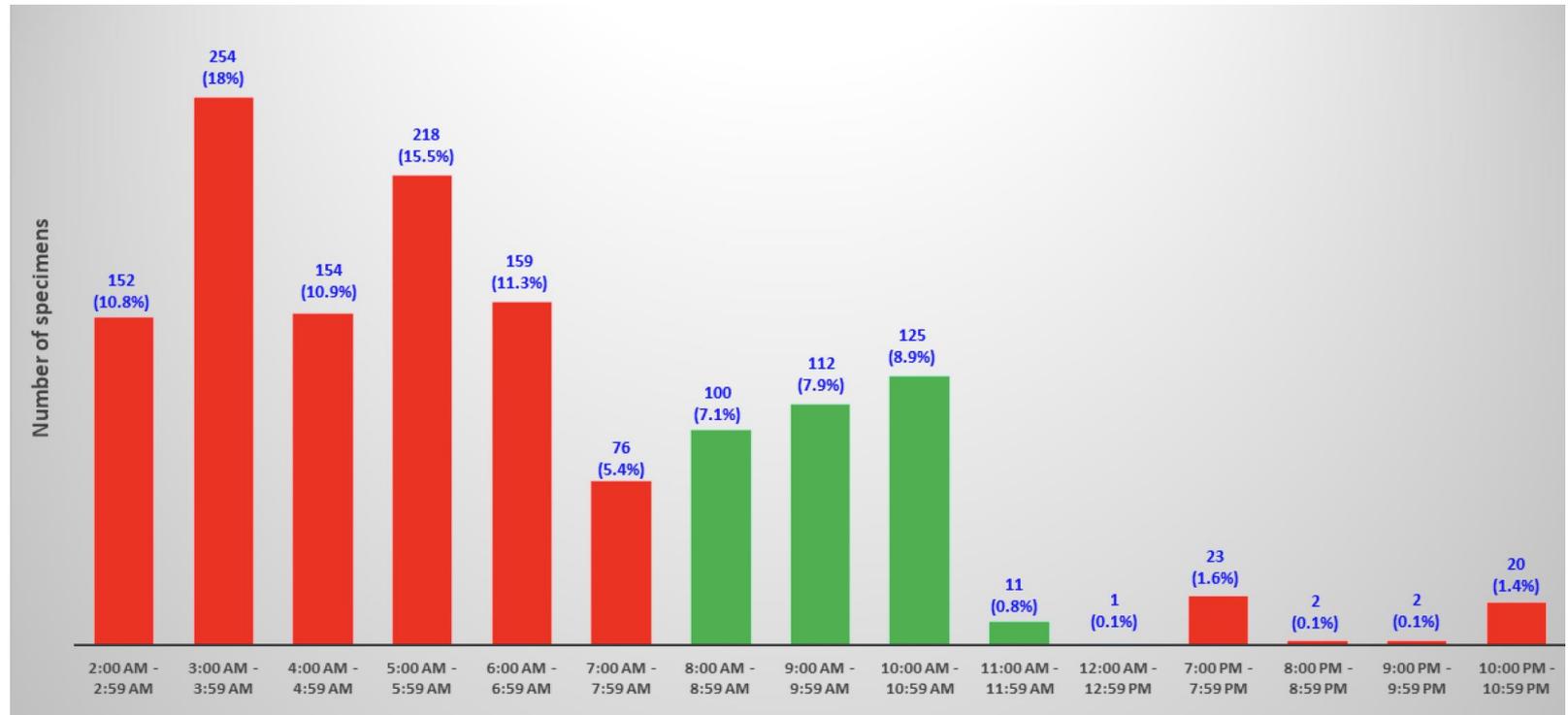
(automated reporting and plate tossing)



Training set: 17'763 samples
Validation set: 1'409 samples

For NEG plates: sens 99.8% / **spec 100%**
For POS plates: sens 100% / spec 92.5%

Releasing NEG MRSA results

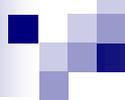


(Cherkaoui A. et al, Clin Microbiol Infect 2019, PMID: **30986560**)
(Cherkaoui A. et al, J Clin Microbiol 2024, PMID: **38126761**)

Table 7 : Definitive incubation protocols 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

		WASPLab		
		Incubation time		
Routine incubation period	Clinical samples type	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



Blood cultures

- Currently no commercially available direct MDx
- Automated blood cultures remain essential!

Blood cultures

- Currently no commercially available direct MDx
- Automated blood cultures remain essential!

Positive bottles:

⇒ MDx

Costly

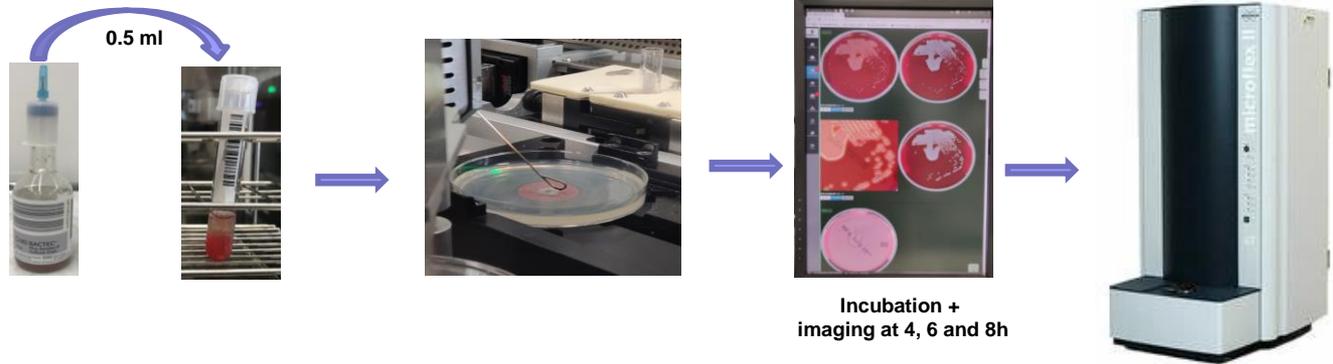
Resistance only for genotypically defined targets

⇒ ID and RAST

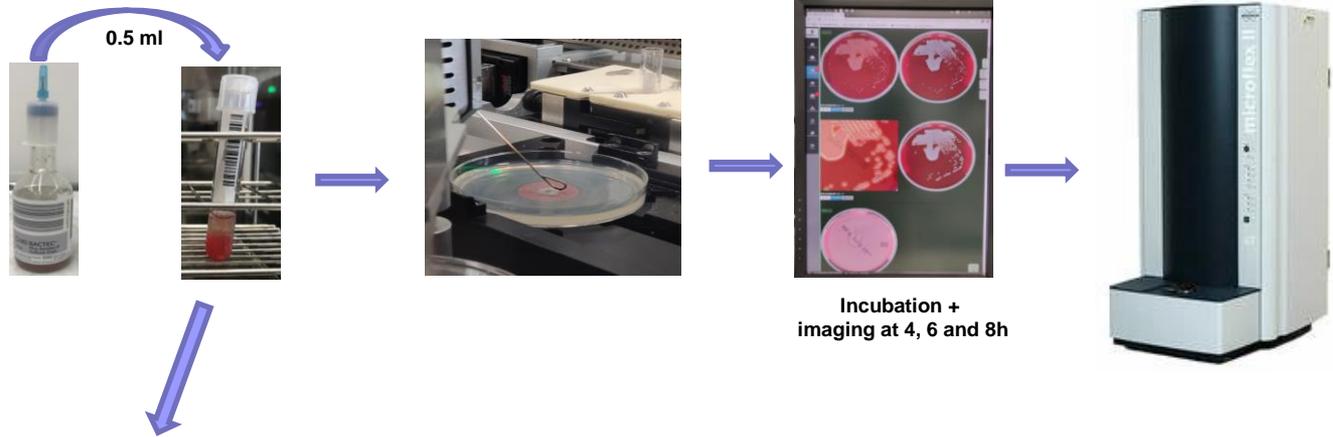
Cheap reagents

Broad susceptibility testing

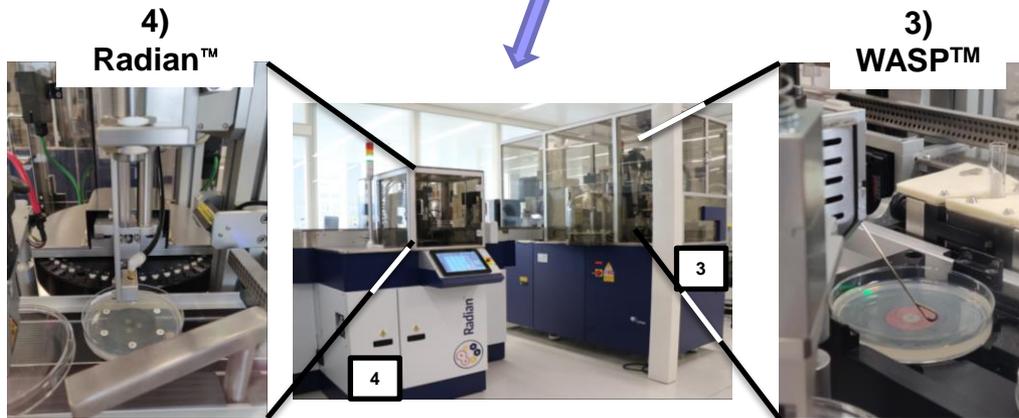
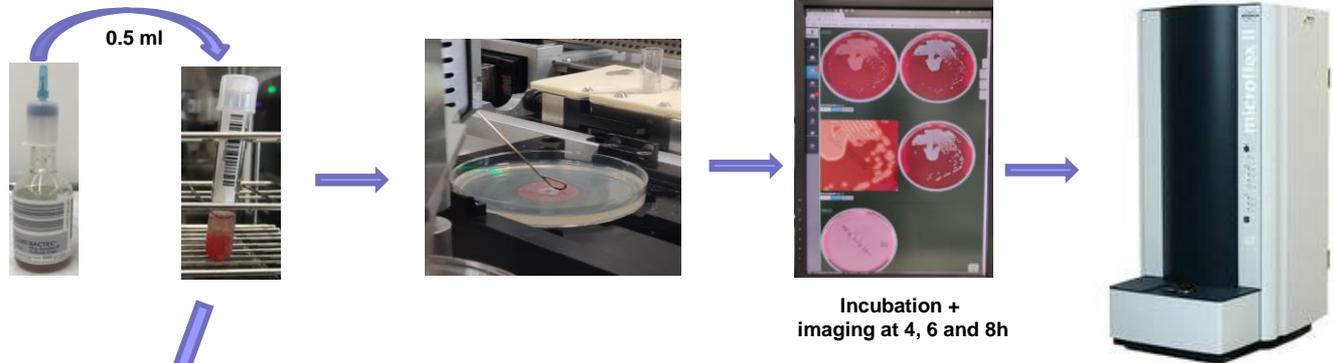
ID on the WASPLab



ID + AST on the WASPLab

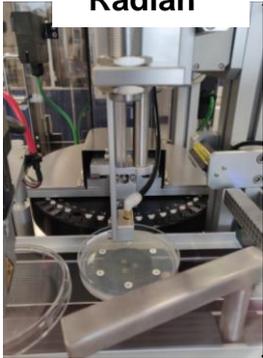


ID + AST on the WASPLab

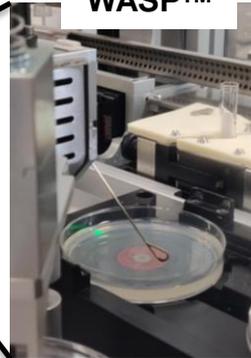


ID + AST on the WASPLab

4)
Radian™

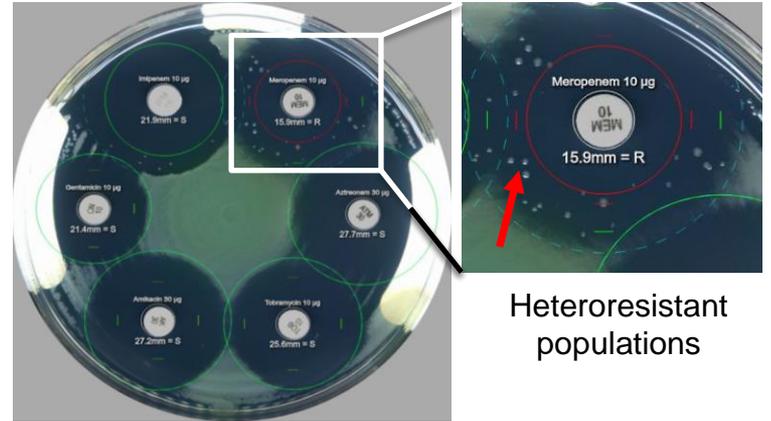


3)
WASP™

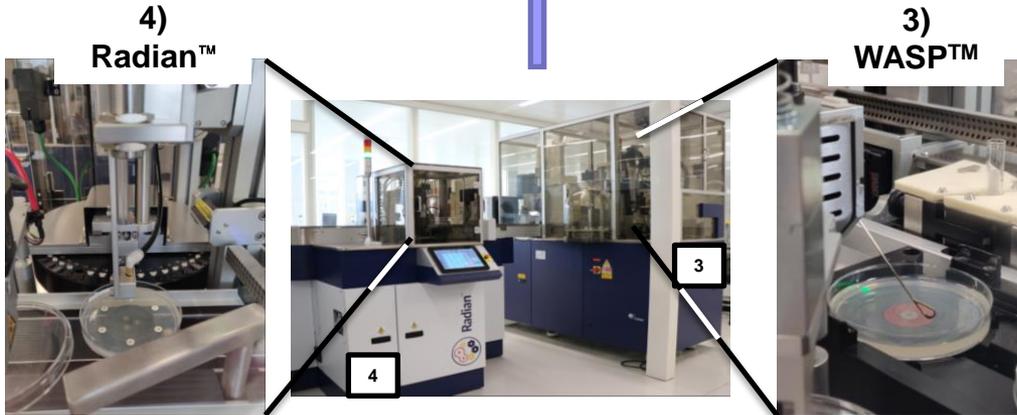




5) WASPLab® AST Line



6) Radian™ Expert System



4) Radian™

3) WASP™

AST on the WASPLab

Comparison of the Copan WASPLab incorporating the BioRad expert system against the SIRscan 2000 automatic for routine antimicrobial disc diffusion susceptibility testing

A. Cherkaoui ^{1,*}, G. Renzi ¹, A. Fischer ¹, N. Azam ¹, D. Schorderet ¹, N. Vuilleumier ^{2,3}, J. Schrenzel ^{1,4}

WASPLab vs SIRScan 2000, using manufacturer's instructions

388 clinical strains (75 MSSA – 19 MRSA – 67 Psaer – 177 ENTB)

Discrepancies resolved by E-tests

AST on the WASPLab

Comparison of the Copan WASPLab incorporating the BioRad expert system against the SIRscan 2000 automatic for routine antimicrobial disc diffusion susceptibility testing

A. Cherkaoui ^{1,*}, G. Renzi ¹, A. Fischer ¹, N. Azam ¹, D. Schorderet ¹, N. Vuilleumier ^{2,3}, J. Schrenzel ^{1,4}

Major errors and very major errors observed with the two compared methods

	No. of strains	Antibiotics tested by strain	Method	Major error	Very major error
<i>Staphylococcus Aureus</i>	94	11	WASPLab	4	0
			SIRscan	1	0
<i>Pseudomonas Aeruginosa</i>	67	12	WASPLab	1	0
			SIRscan	3	3
<i>Enterobacterales</i>	177	16	WASPLab	26	0
			SIRscan	3	5

AST on the WASPLab

Comparison of the Copan WASPLab incorporating the BioRad expert system against the SIRscan 2000 automatic for routine antimicrobial disc diffusion susceptibility testing

A. Cherkaoui ^{1,*}, G. Renzi ¹, A. Fischer ¹, N. Azam ¹, D. Schorderet ¹, N. Vuilleumier ^{2,3}, J. Schrenzel ^{1,4}

Major errors and very major errors observed with the two compared methods

	No. of strains	Antibiotics tested by strain	Method	Major error	Very major error
<i>Staphylococcus Aureus</i>	94	11	WASPLab	4	0
			SIRscan	1	0
<i>Pseudomonas Aeruginosa</i>	67	12	WASPLab	1	0
			SIRscan	3	3
<i>Enterobacterales</i>	177	16	WASPLab	26	0
			SIRscan	3	5

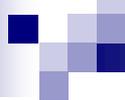
AST on the WASPLab

Comparison of the Copan WASPLab incorporating the BioRad expert system against the SIRscan 2000 automatic for routine antimicrobial disc diffusion susceptibility testing

A. Cherkaoui ^{1,*}, G. Renzi ¹, A. Fischer ¹, N. Azam ¹, D. Schorderet ¹, N. Vuilleumier ^{2,3},
J. Schrenzel ^{1,4}

Major errors due to the disks (variable dosage or heat labile?)

Disks loaded on WASPLab for 16 hours only (kept at 4°C)



AST on the WASPLab II

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}

September 2021 Volume 59 Issue 9 e00777-21

Journal of Clinical Microbiology

Comparison *versus* Vitek 2

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				
Piperacillin/Tazobactam	21 (62)	98.6				
Cefuroxime	25 (73)	100				
Ceftazidime	22 (63)	99.3				
Ceftriaxone	22 (63)	99.3				
Cefepime	19 (56)	99				
Imipenem	6 (18)	98.6				
Meropenem	7 (19)	99.7				
Ertapenem	17 (49)	97.6				
Amikacin	7 (19)	99.7				
Gentamicin	15 (45)	99.7				
Norfloxacin	35 (101)	100				
Ciprofloxacin	29 (85)	99.3				
Co-trimoxazole	35 (103)	99.7				

Strains selected

44/292 (15%) ESBL

43/292 (15%) CPE

7 NDM

3 KPC

16 Oxa-48

17 Oxa-181

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		
				15	12	3

The overall categorical agreements between the two compared methods

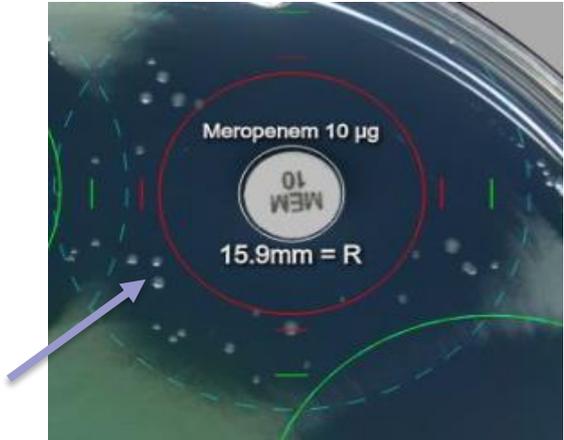
99.3% (4350/4380; 95% CI 99% to 99.5%)

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		
<i>Pseudomonas aeruginosa</i> (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*)	

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%)



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

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
<i>Staphylococcus</i> spp. (n=185 including 107 <i>Staphylococcus aureus</i> and 78 Coagulase-negative staphylococci)						
Cefoxitine	32 (60)	100			1	
Gentamicin	21 (39)	100				
Ciprofloxacin	32 (60)	99.5				
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				

The overall categorical agreements between the two compared methods

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

AST on the WASPLab II

Radian in WASPLab		Vitek 2	
Fully automated	✓	Semi-automated	
Easy to change the selected AB disks	✓	Need to order new cards	
Detects hetero-resistance	✓	Poor detection of hetero-resistance	
Easy detection of mixed cultures	✓	Requires purity plates	
Better detection of some CPE (OXA-48)	✓		
Greatest flexibility and cost effectiveness	✓		
Cannot provide estimates of MICs		Good approximation of MICs	✓

97% of routine AST switched to the Colibri coupled to Radian within 5 months (100 to 150 AST panels per day / 350 to 420 plates per day)



Need for (more) speed?

Rapid AST:

Jonasson et al. J Antimicrob
Chemother 2020; 75:
968–978

NOT readable inhibition
zones %

	Strains number	Number of tests	4h	6h	8h
<i>Escherichia coli</i>	60	958	8.0		
<i>Klebsiella pneumoniae</i>	52	831	1.0		
<i>Pseudomonas aeruginos</i>	53	741		9.0	2.0
<i>Staphylococcus aureus</i>	54	432	42.0	21.0	9.0
<i>Enterococcus faecalis</i>	23	260	7.0		
<i>Enterococcus faecium</i>	34	380	100.0	7.0	1.0
<i>Acinetobacter baumannii</i>			No data available		

Rapid AST: RAST on the WASPLab

Cherkaoui et al. 2022

Jonasson et al. J Antimicrob Chemother 2020; 75: 968–978

NOT readable inhibition zones %

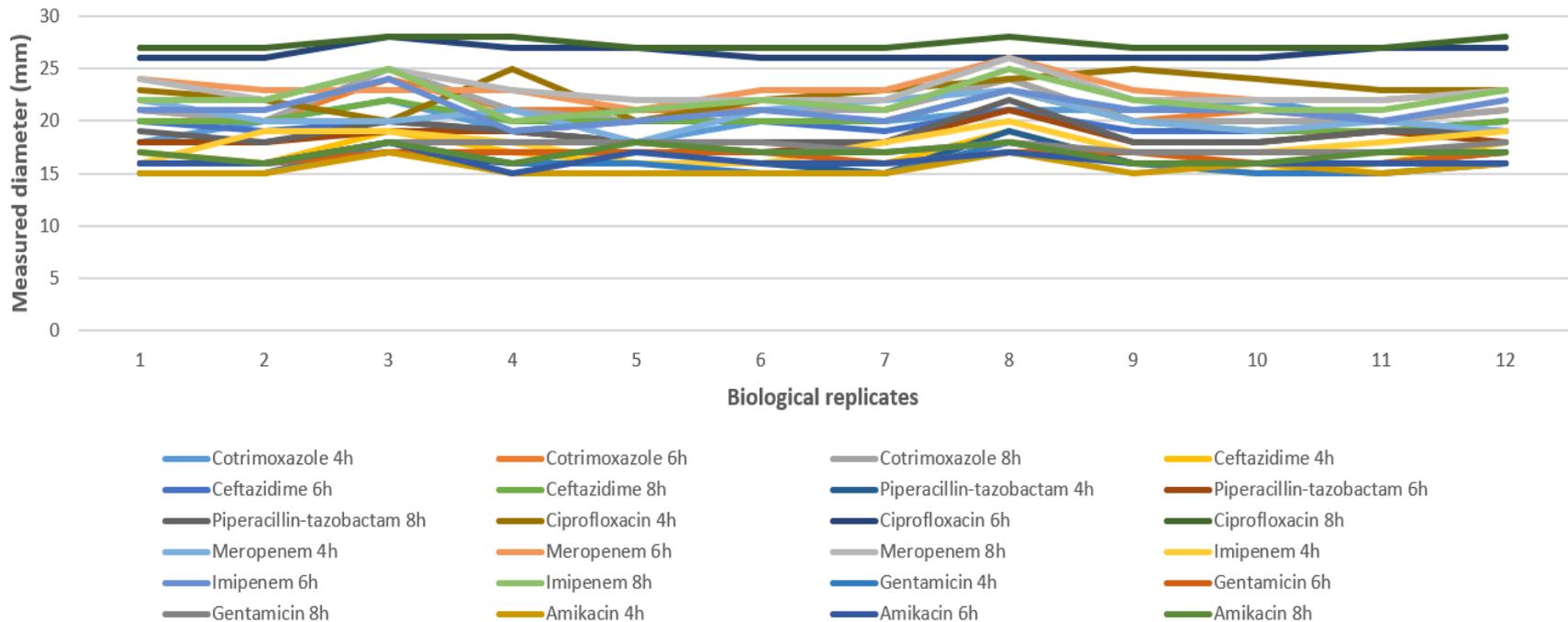
NOT readable inhibition zones %

	Number of isolates	Number of tests	4h	6h	8h	Strains number	Number of tests	4h	6h	8h
<i>Escherichia coli</i>	306	2448	2.9			60	958	8.0		
<i>Klebsiella pneumoniae</i>	161	1288	0.6			52	831	1.0		
<i>Pseudomonas aeruginosa</i>	129	1161		3.1		53	741		9.0	2.0
<i>Staphylococcus aureus</i>	228	912	9.1			54	432	42.0	21.0	9.0
<i>Enterococcus faecalis</i>	89	445	9.2			23	260	7.0		
<i>Enterococcus faecium</i>	47	235				34	380	100.0	7.0	1.0
<i>Acinetobacter baumannii</i>	63	441	3.2			No data available				

(Jonasson E et al, J Antimicrob Chemother 2020, PMC: **7069491**)
 (Cherkaoui A et al, J Clin Microbiol. 2022, PMID: **36173195**)

Quality controls for RAST: within published range

E. coli ATCC 25922



Clinical impact of RAST?

Reduced TAT in the lab ✓

Rapid results transmission ✓

Rapid AB change?

Real de-escalation?

Objective metrics

=> quantification and comparison

Clinical impact of RAST?

scientific reports

OPEN

Simplified Spectrum Score (S^3) app for pathogen-agnostic antimicrobial drug spectrum ranking to assess for antimicrobial de-escalation events

Mikaël de Lorenzi-Tognon^{1,2} & Jacques Schrenzel^{1,2,3}

Antimicrobial/antibiotic de-escalation (ADE) is a key feature of antimicrobial stewardship programs (ASP) that relies mainly on individual panels for determining ADE events based on subjective ranking of antibiotics' spectrum activity. The lack of consensus among ASP experts leads to reproducibility issues in the measure of this clinical outcome, making difficult to assess its real impact on patient care. The S^3 score (Simplified Spectrum Score) app was developed to allow an objective ranking of antibiotics. Ranking was achieved by developing a database harboring pairs of bacteria-antibiotics for which each molecule was assigned a score based on published and clinically validated data from a recognized international committee. S^3 score shows a strong correlation relationship and substantial agreement to a clinically validated spectrum score, and its framework enables any person to use it for ADE detection without assuming prior knowledge or training. In addition, its design enables regular updates and sustainability.

11:56



Simplified Spectrum Score – S^3 score

- [S³ score calculator](#)
- [Methodology](#)
- [Drug Score List](#)
- [About](#)

ADE assessment with S³ App (1)

Empirical (initial) antimicrobial therapy

- Meropenem

Targeted (final) antimicrobial therapy

- Amoxicillin-clavulanate

The image displays two screenshots of the S³ App interface. The left screenshot shows the 'Simplified Spectrum Score (S3score)' screen with two sections: 'Choose initial antimicrobial therapy' and 'Choose final antimicrobial therapy'. In the initial therapy section, 'Antimicrobial n°1' is set to 'meropenem' and 'Antimicrobial n°2' is set to 'none'. In the final therapy section, 'Antimicrobial n°6' is set to 'amoxicillin_clavulanate' and 'Antimicrobial n°7' is set to 'none'. A red arrow points to the 'S3score' button at the bottom. The right screenshot shows the result screen with the following information: 'INITIAL ANTIMICROBIAL DRUG(S): meropenem' with a score of 90.68 (0-100 scale); 'FINAL ANTIMICROBIAL DRUG(S): amoxicillin_clavulanate' with a score of 31.54 (0-100 scale); 'DELTA S³ SCORE: -59.14'; and 'OUTCOME: De-escalation was successful !'. A red arrow points from the 'S3score' button in the left screenshot to the result screen.

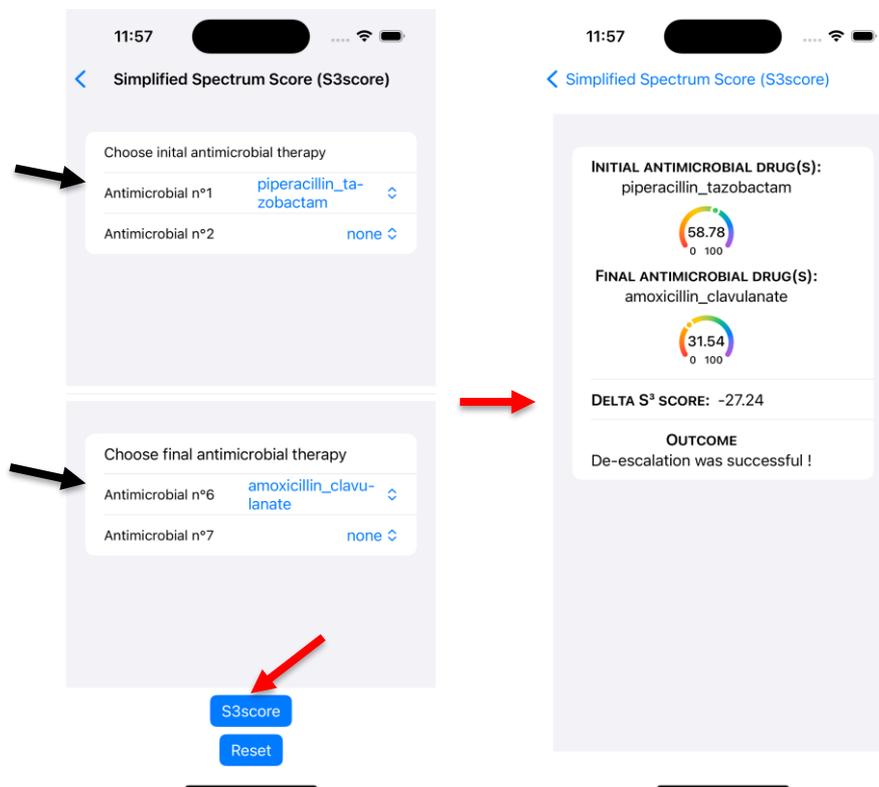
ADE assessment with S³ App (2)

Empirical (initial) antimicrobial therapy

- Piperacillin-tazobactam

Targeted (final) antimicrobial therapy

- Amoxicillin-clavulanate



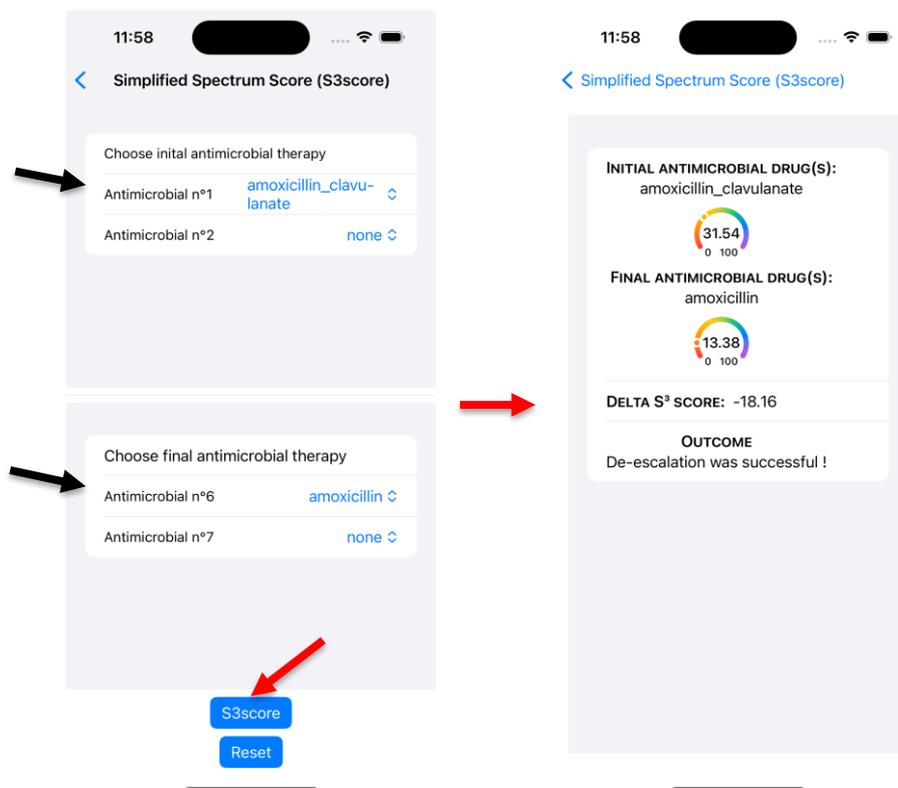
ADE assessment with S³ App (3)

Empirical (initial) antimicrobial therapy

- Amoxicillin-clavulanate

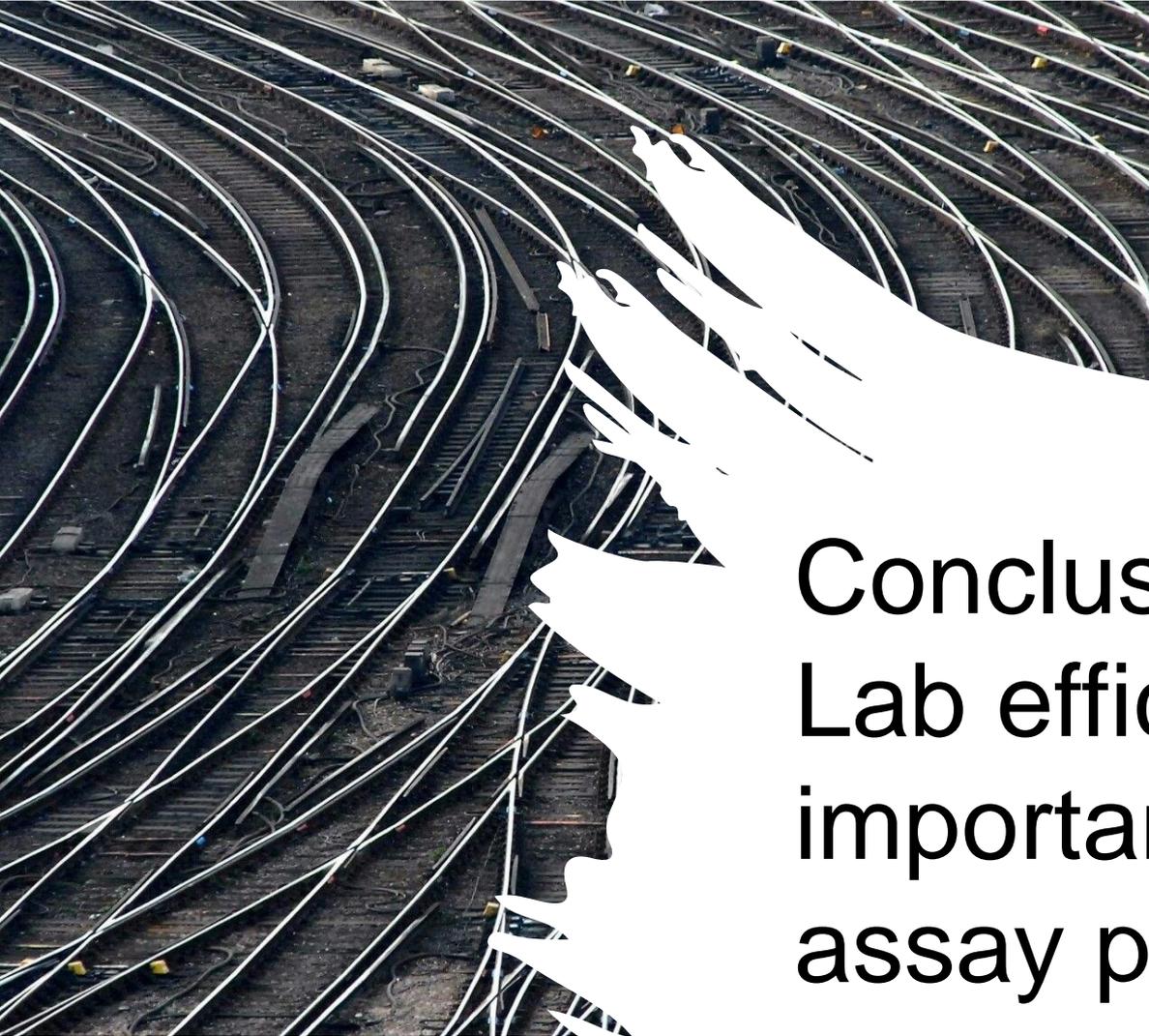
Targeted (final) antimicrobial therapy

- Amoxicillin



Conclusion





**Conclusion:
Lab efficiency is more
important than single
assay performance**