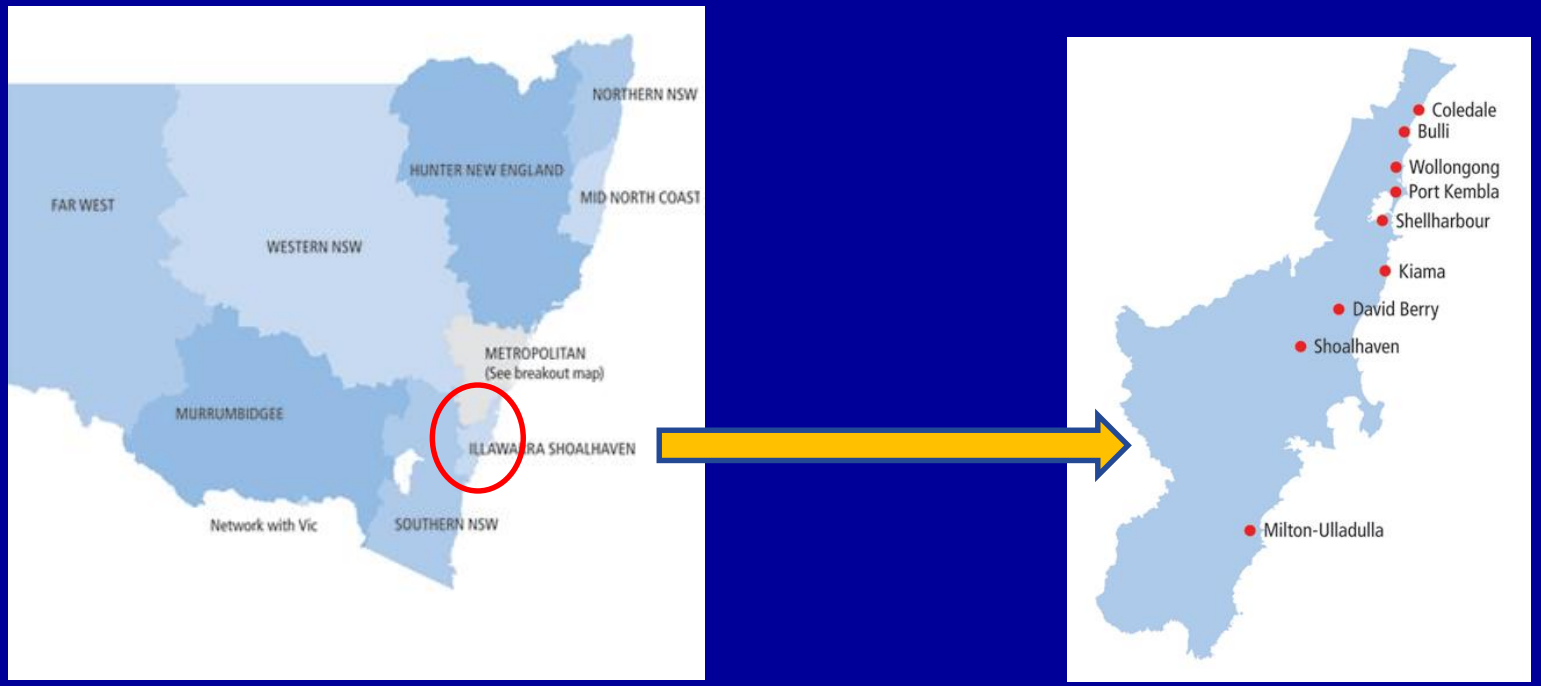
Why the CDS?

The unique advantages of using an Australian antimicrobial susceptibility testing method

Peter Newton
Medical Microbiologist
Wollongong Hospital, Wollongong, NSW

Where do I come from?

- SEALS South Microbiology/Serology Dept.
- Serve the 9 hospitals of the Illawarra Shoalhaven Local Health District



Our major hospitals

- Wollongong Hospital
  - 200-500 beds
  - >47,500 admissions 2010-2011
  - >51,000 ED presentations 2011-2012
- Shoalhaven Hospital, Nowra
  - 100-200 beds
  - >21,500 admissions 2010-2011
  - >34,000 ED presentations 2011-2012
- Shellharbour Hospital
  - 100-200 beds
  - >17,500 admissions 2010-2011
  - >25,000 ED presentations 2011-2012

Source: http://www.myhospitals.gov.au/

Our laboratory

- Staff establishment
  - 1 FTE lab manager (Principal Scientist)
  - 1 FTE Senior Scientist Microbiology
  - 1 FTE Senior Scientist Serology
  - 2 FTE Scientific Officers
  - 10.5 FTE Technical Officers
  - 1 FTE Technical Assistant
- Workload:
  - Urines in 2012: 32,857 (10% ↑ from 2011)
  - Blood cultures in 2012: 16,590 (17%↑ from 2011)
- User of CDS method >30 years

Who else uses the CDS method?

- CDS Users registrants from
  - All Australian states & territories except S.A.
  - Internationally
    - Singapore, Malaysia, Thailand, Vietnam, Hong Kong, India
    - South Africa, Saudi Arabia
    - Spain, France, USA

- RCPA QAP participant data
  - 2012:8 Urine *E. coli* 50/277 (18%) respondents
  - 2012:8 Urine *C. urealyticum* 57/195 (29%) respondents
  - 2012:8 Skin *S. aureus* 48/254 (19%) respondents

Source: Deb Walker, Senior Scientist, RCPA Microbiology QAP

Unique advantages of the CDS method

- Simplicity
  - Inoculum preparation
  - Ease of interpretation
  - Applicable to labs of all sizes & experience/skill mix
- Optimised for sensitivity of resistance detection; specificity of “susceptible” results
  - M.I.C. & inhibitory zone cut-offs
  - Disc potencies
- Lower cost than some other methods

Unique advantages of the CDS method

- Australian method in use >35 years
- Validated on Australian and overseas strains
  - Collaboration with overseas labs
  - Correlation with molecular methods for some resistance mechanisms
- Free internet access to
  - Method manual
  - Regular updates
  - Newsletters or notifications e-mailed to registered users to advise of changes

These documents cost me $AUS 670

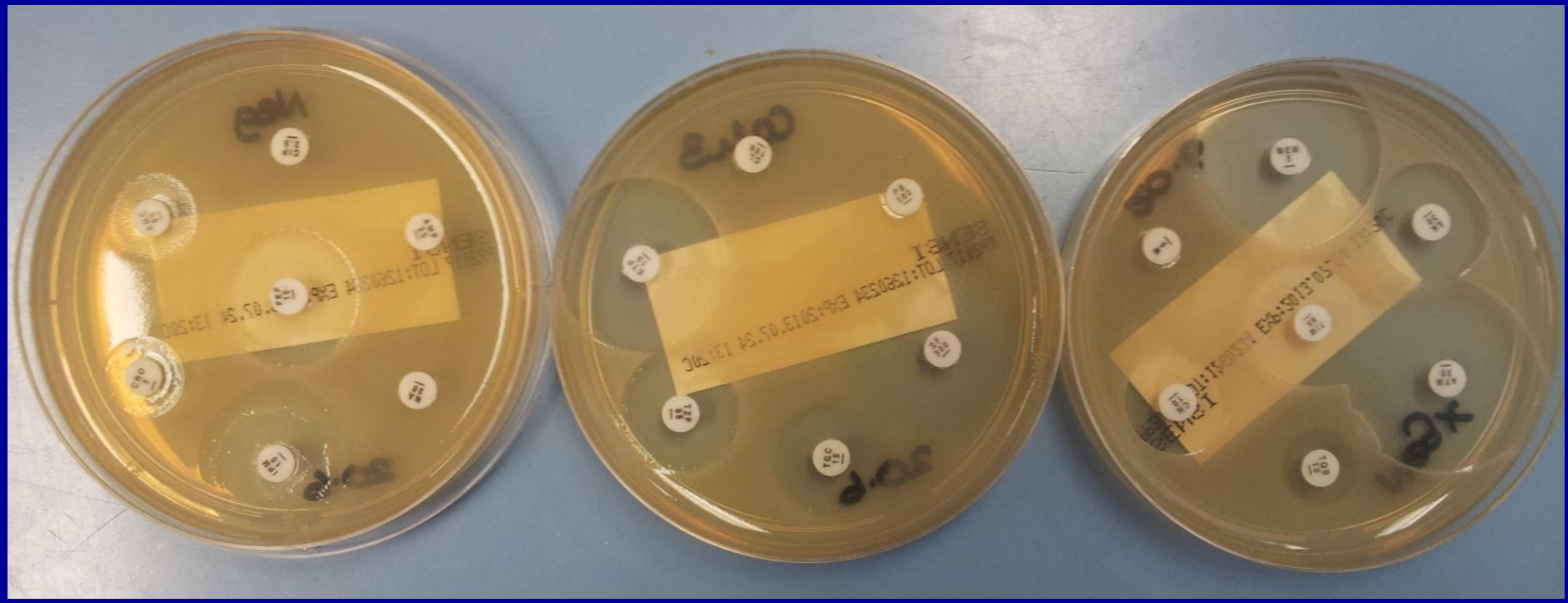
Unique advantages of the CDS method

- Free access to a local (Australian) reference laboratory
  - Prompt advice & feedback (phone & e-mail)
  - Interpret antibiograms & digital images
  - Happy to receive isolates for further phenotypic and molecular confirmatory testing
  - Provision of certified reference strains for QC
  - Response to user feedback & requests
    - New antibiotic calibrations
- Yearly user group workshops
  - Method updates, new & unusual resistances

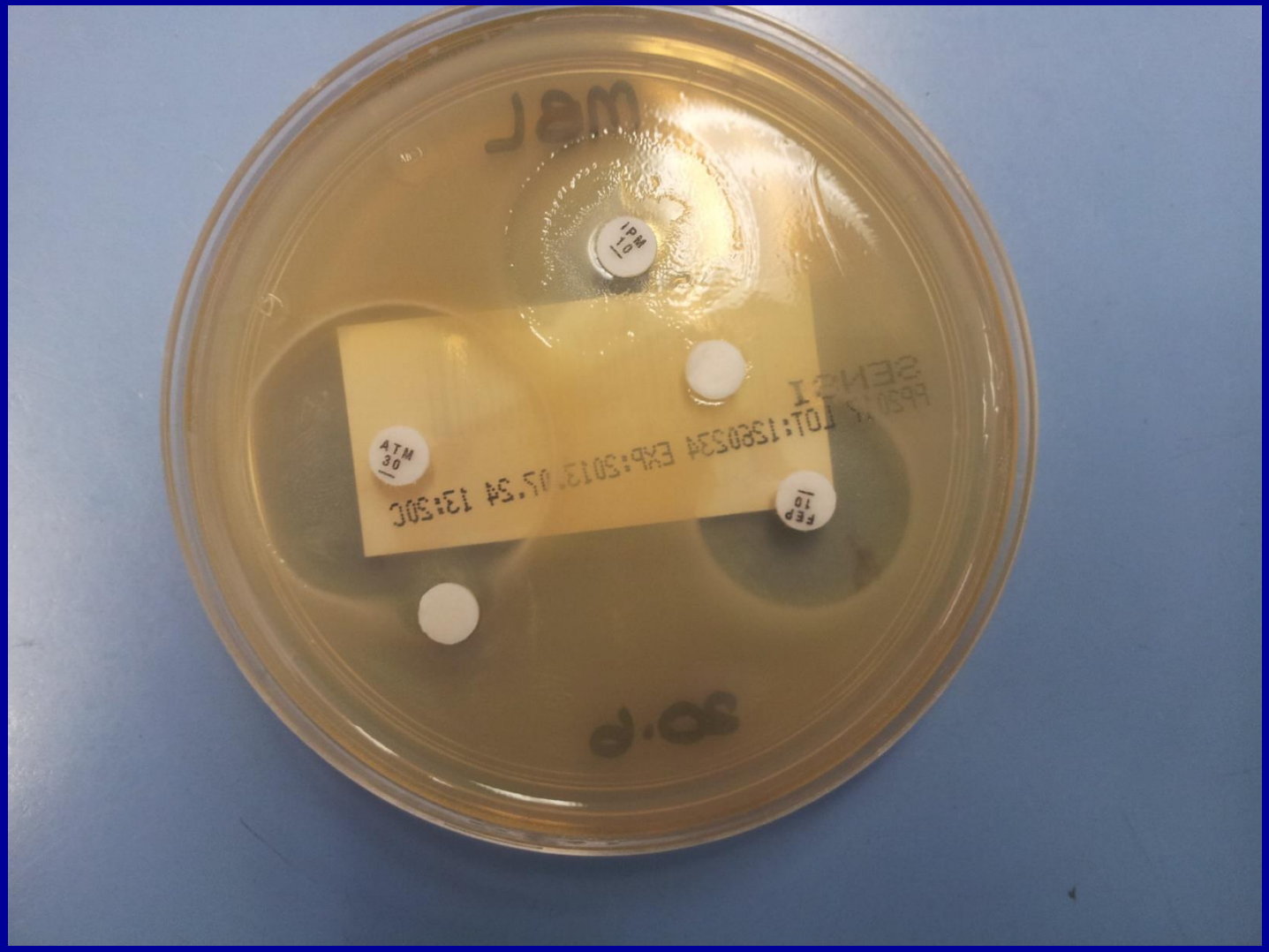
SEALS South recent use of CDS reference lab – case 1

- 84 y.o. male NH patient presented in late May 2013 with sepsis
- Blood cultures and CSU grew *Proteus mirabilis*
  - Resistant to Ampicillin, Cephalexin, Ceftriaxone
  - Sensitive to Cefepime and Aztreonam
  - ESBL and MBL phenotypic tests negative
- Unusual for SEALS South: no prior CRO resistance in *P. mirabilis* without ESBL or MBL

SEALS South recent use of CDS reference lab – case 1



SEALS South recent use of CDS reference lab – case 1



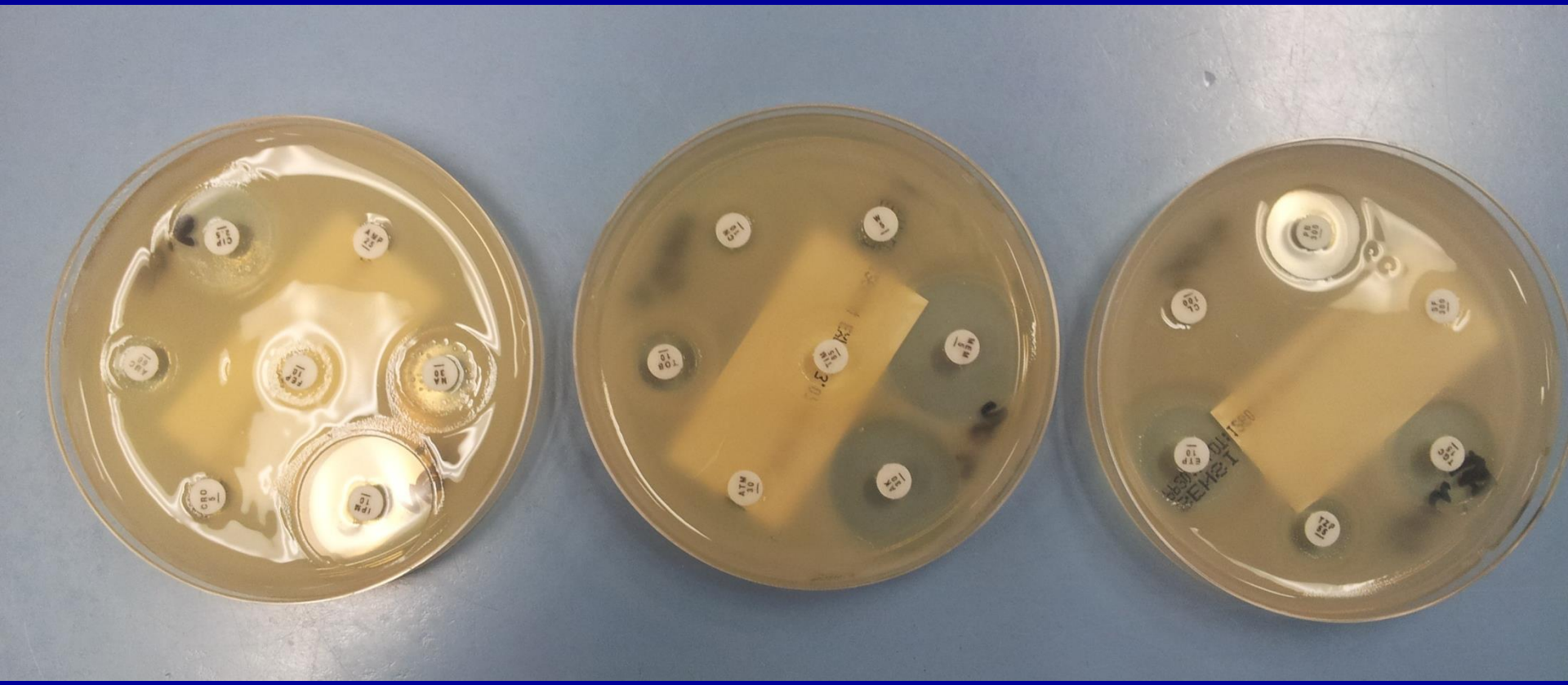
SEALS South recent use of CDS reference lab – case 1

- E-mail response from CDS reference lab within 1 working day
  - Phenotypic tests suggest high activity plasmid-mediated AmpC cephalosporinase
    - (R) Ampicillin, Augmentin, Cephalexin, Cefotaxime, Cefoxitin, Ceftazidime
    - (S) to Cefepime and Aztreonam
    - Synergy between boronic acid and Ceftazidime
  - PCR positive for DHA-1, DHA-2 genes (AmpC)

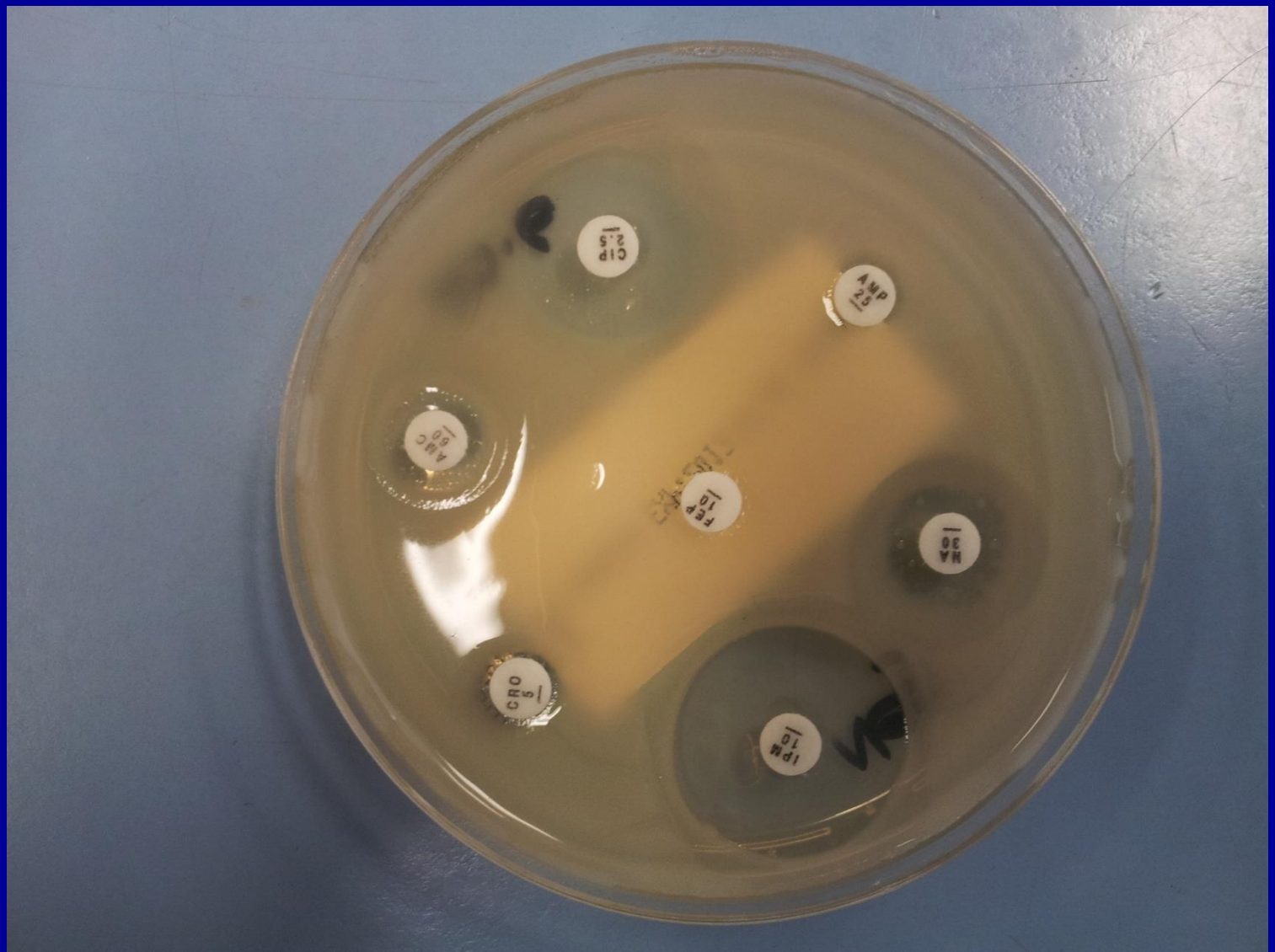
SEALS South recent use of CDS reference lab – case 2

- 72 y.o. male with a complicated AAA graft infection and aortoenteric fistula
- Nosocomial sepsis with blood cultures growing mucoid *Enterobacter cloacae*

SEALS South recent use of CDS reference lab – case 2



SEALS South recent use of CDS reference lab – case 2



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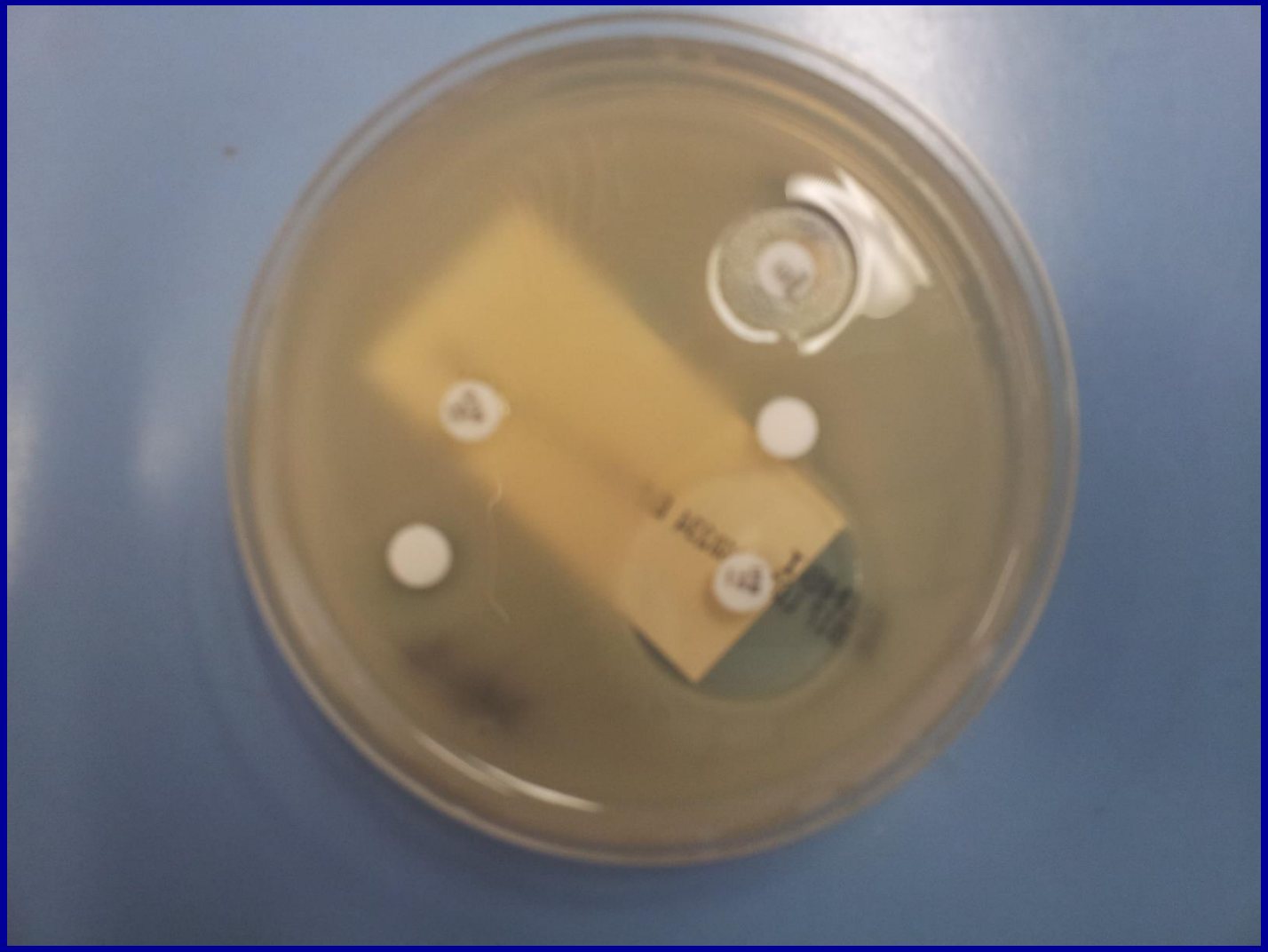


SEALS South recent use of CDS reference lab – case 2

- E-mail response from CDS reference lab within 1 day:
  - Multiplex PCR negative for carbapenemase genes
  - SHV-5 gene detected (ESBL)

Detection of Carbapenem Resistant *Enterobacteriaceae* (CRE) in Australia

- Australian Commission on Safety and Quality in Health Care
  - Draft recommendations for the control of Multi drug resistant Gram negatives: carbapenem resistant *Enterobacteriaceae*, April 2013

- Ginn AN, Partridge SR, Iredell JR. Detection of carbapenemase enzymes in the *Enterobacteriaceae*. Breakpoint (ASA Newsletter) 2013 – Issue 03

Carbapenemases of concern in *Enterobacteriaceae*

- Metallo-β-lactamases (MBLs)
  - Ambler class B (inhibited by EDTA)
  - IMP, NDM, VIM etc.
- KPCs (Klebsiella pneumoniae carbapenemases)
  - Ambler class A (inhibited by clavulanic acid)
- OXA-48 and 48-like (OXA-181)
  - Ambler class D
  - Partially inhibited by clavulanic acid

CDS method and Carbapenemase Detection

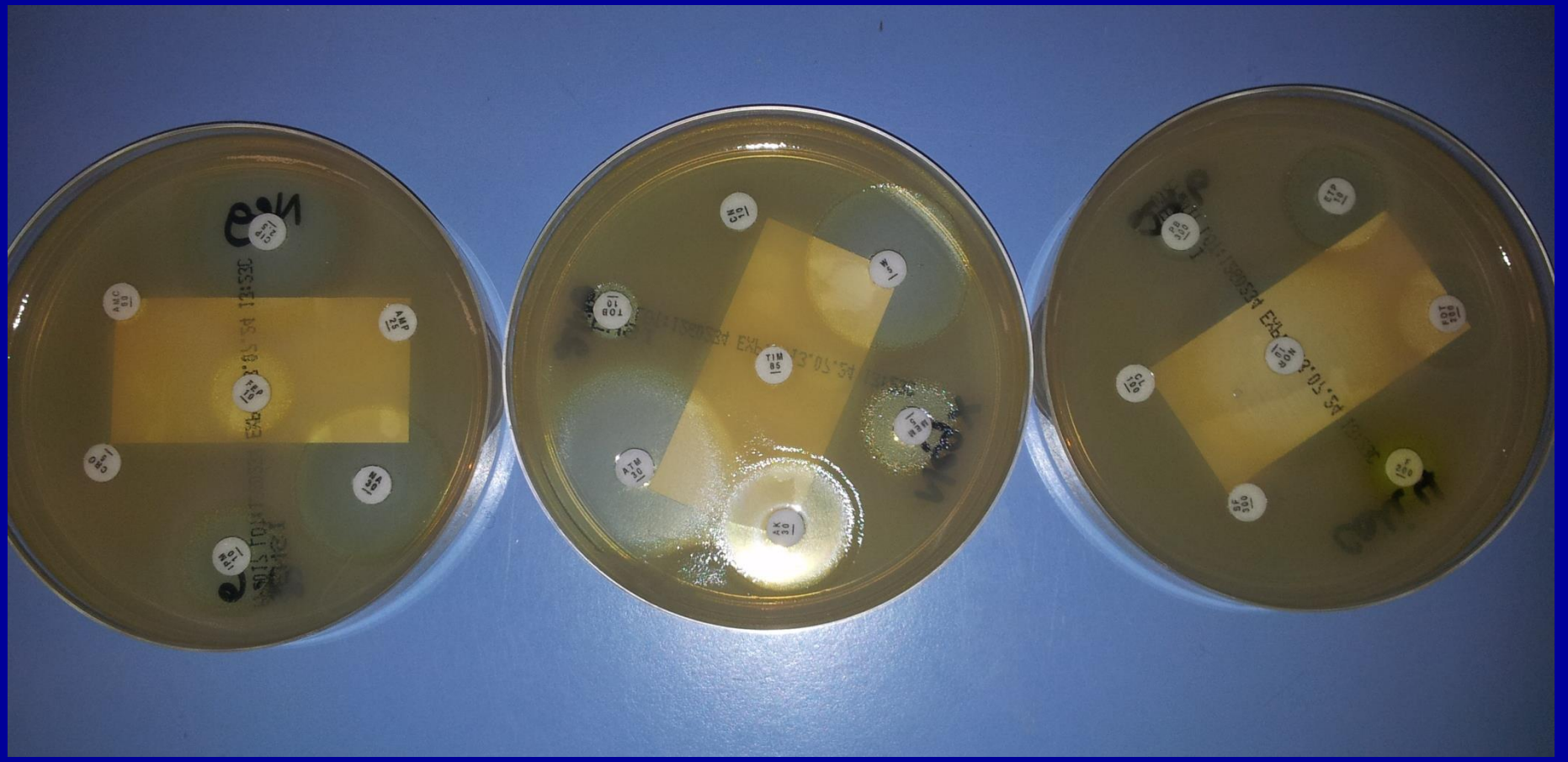
- MBL detection
  - Discussed at yearly CDS workshops since 2003
  - Covered in CDS Manual since 3rd ed 2004

- KPC detection
  - First discussed at CDS workshop ASM 2009
  - Covered in CDS Manual since 6th ed 2011

CRE Isolates SEALS South 2011-June 30 2013

	2011	2012	2013 to June 30	Total
No. of isolates	16	16	19	51
No. of patients	14	13	14	41
Carbapenemase	15	13	18	46
IMP	15	13	18	46
+ ESBL	4	2	3	9

SEALS South *Serratia marcescens* isolate from nephrostomy urine April 2013



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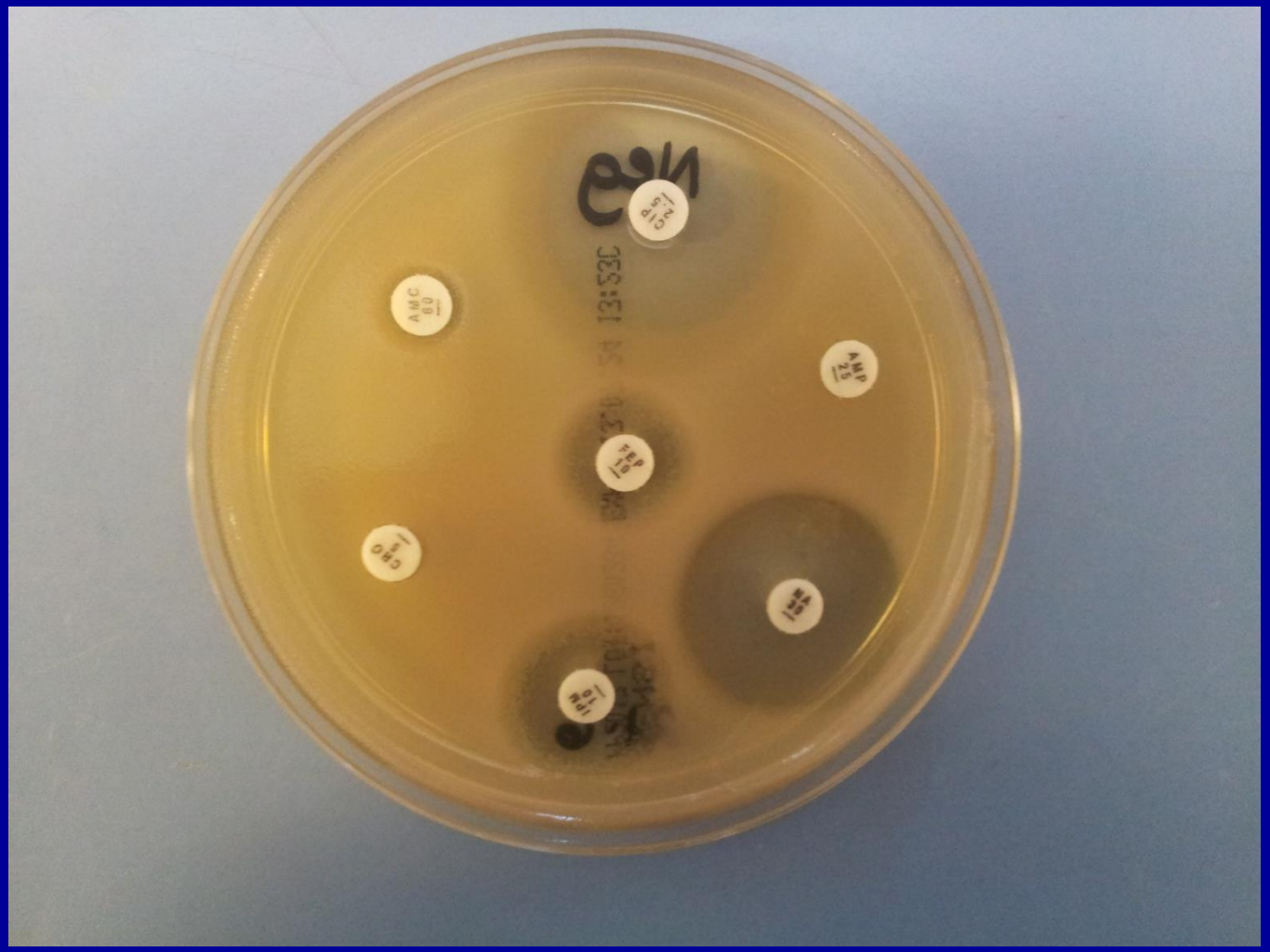

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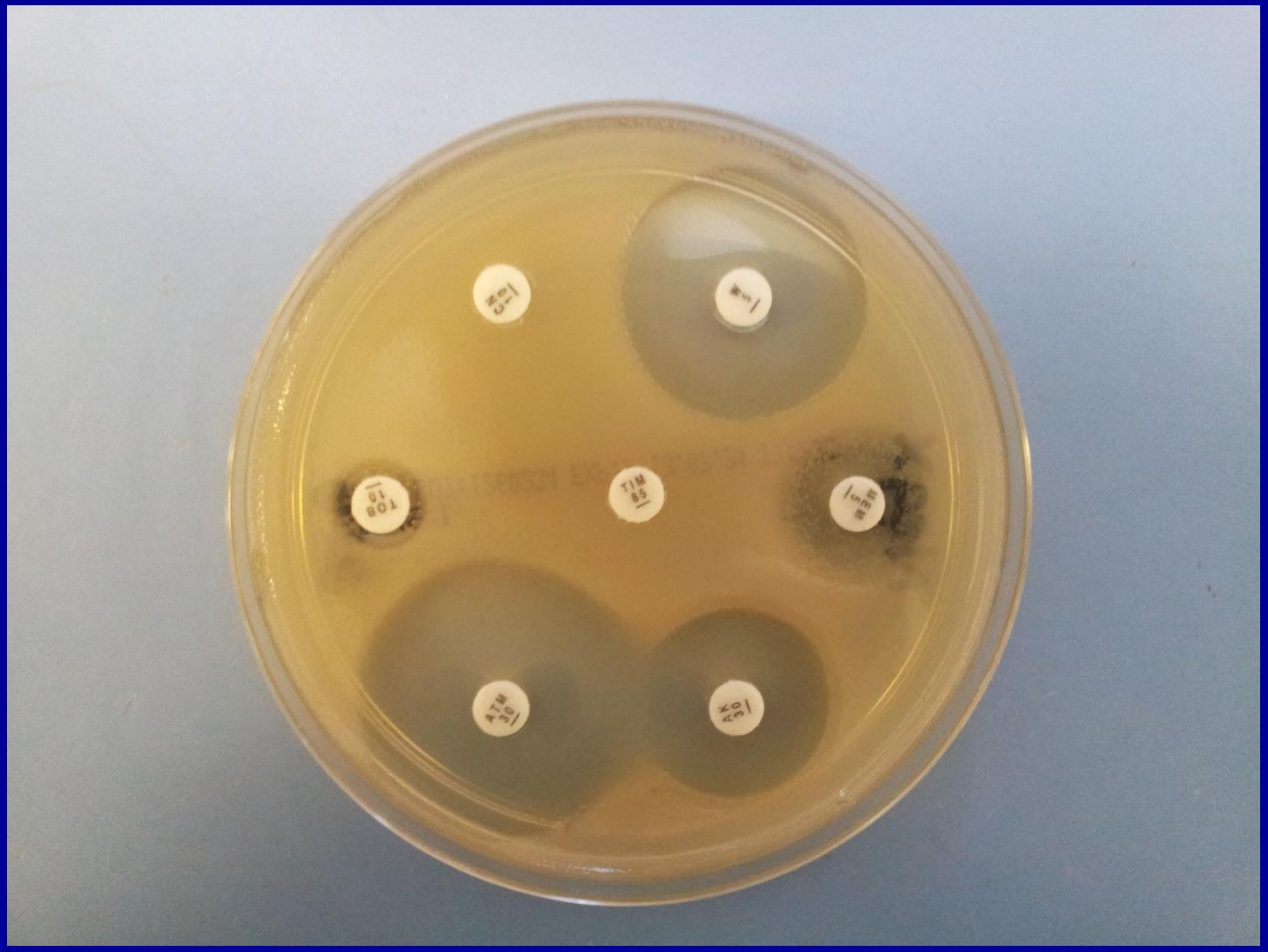

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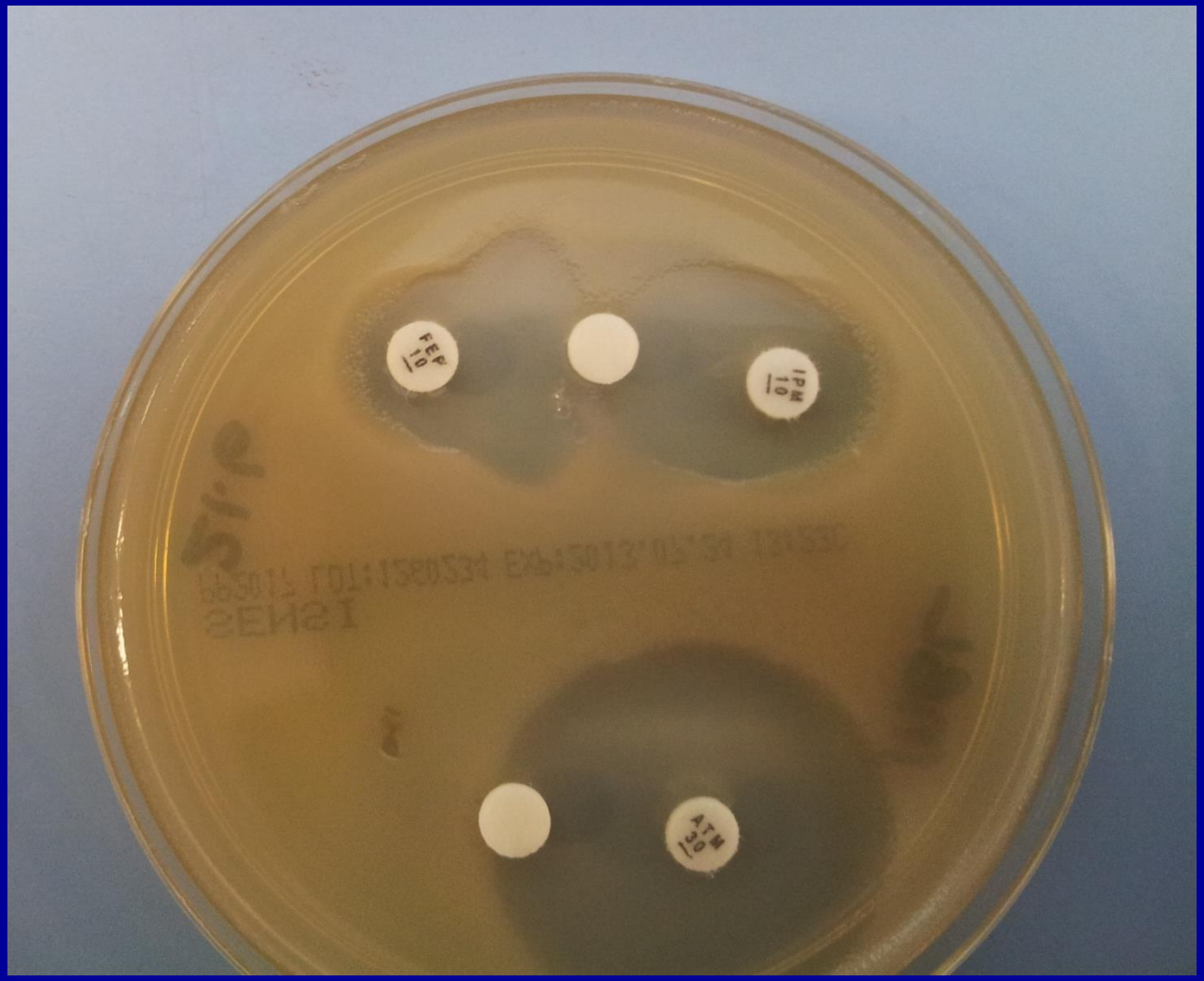
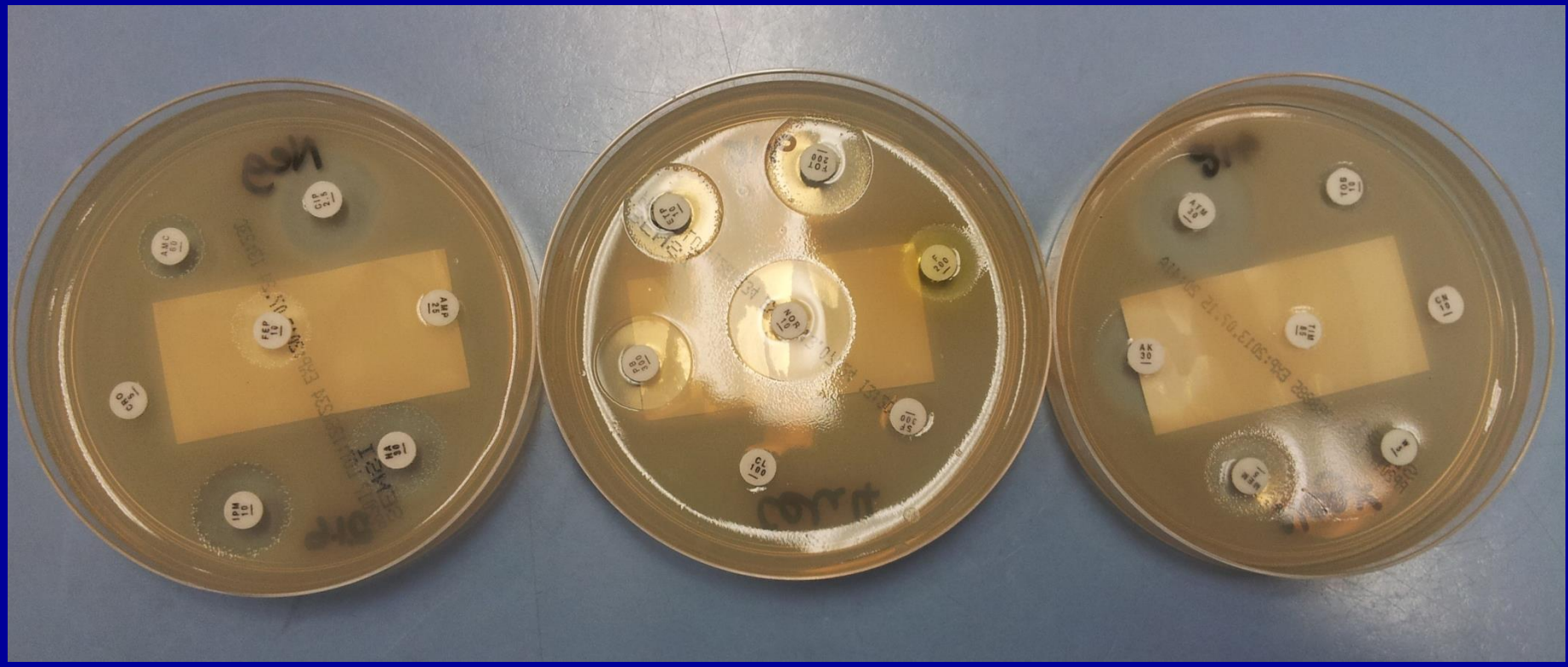
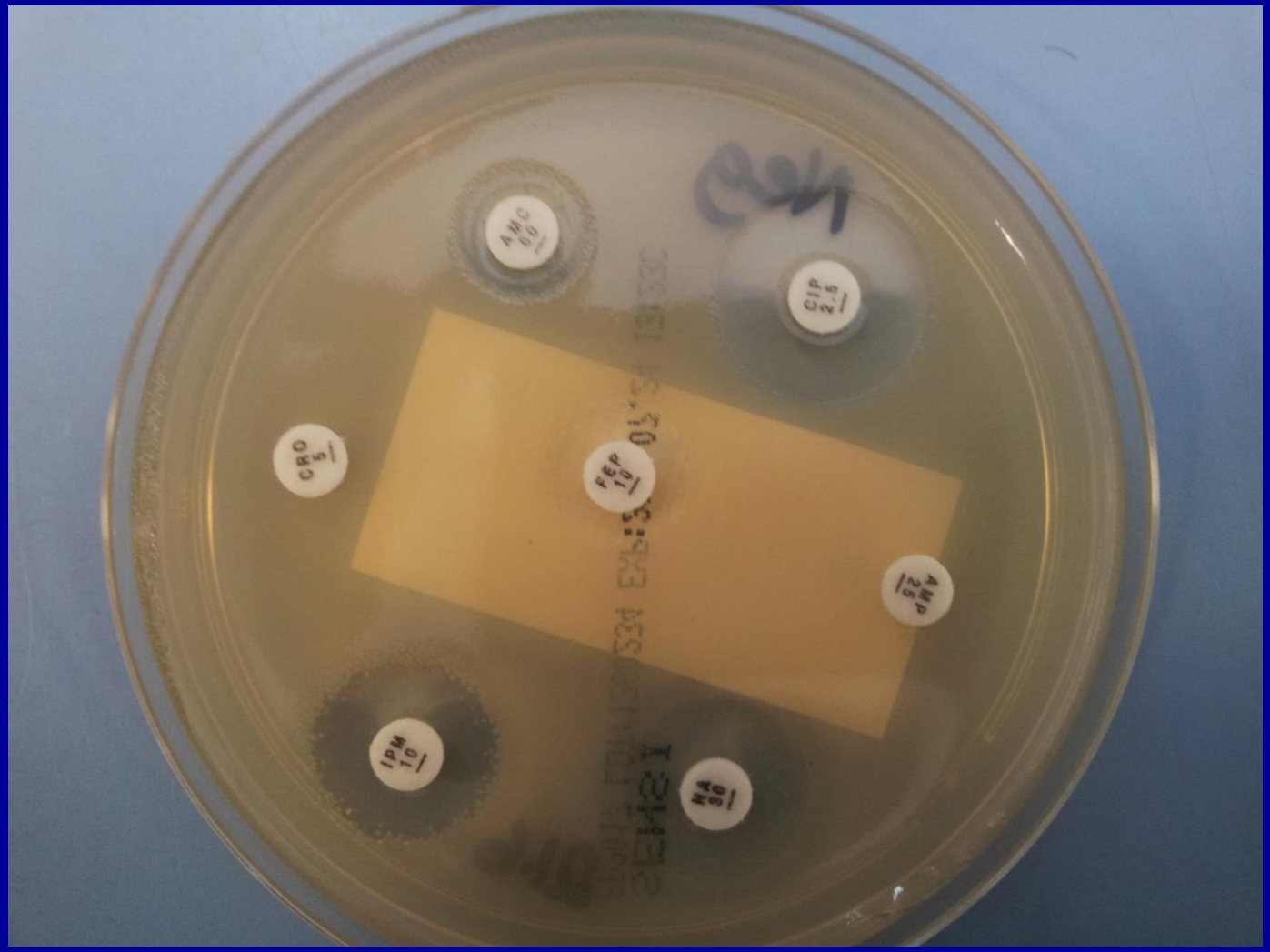


PCR: IMP +ve

SEALS South *Enterobacter cloacae* isolate from catheter urine May 2013



SEALS South *Enterobacter cloacae* isolate from catheter urine May 2013



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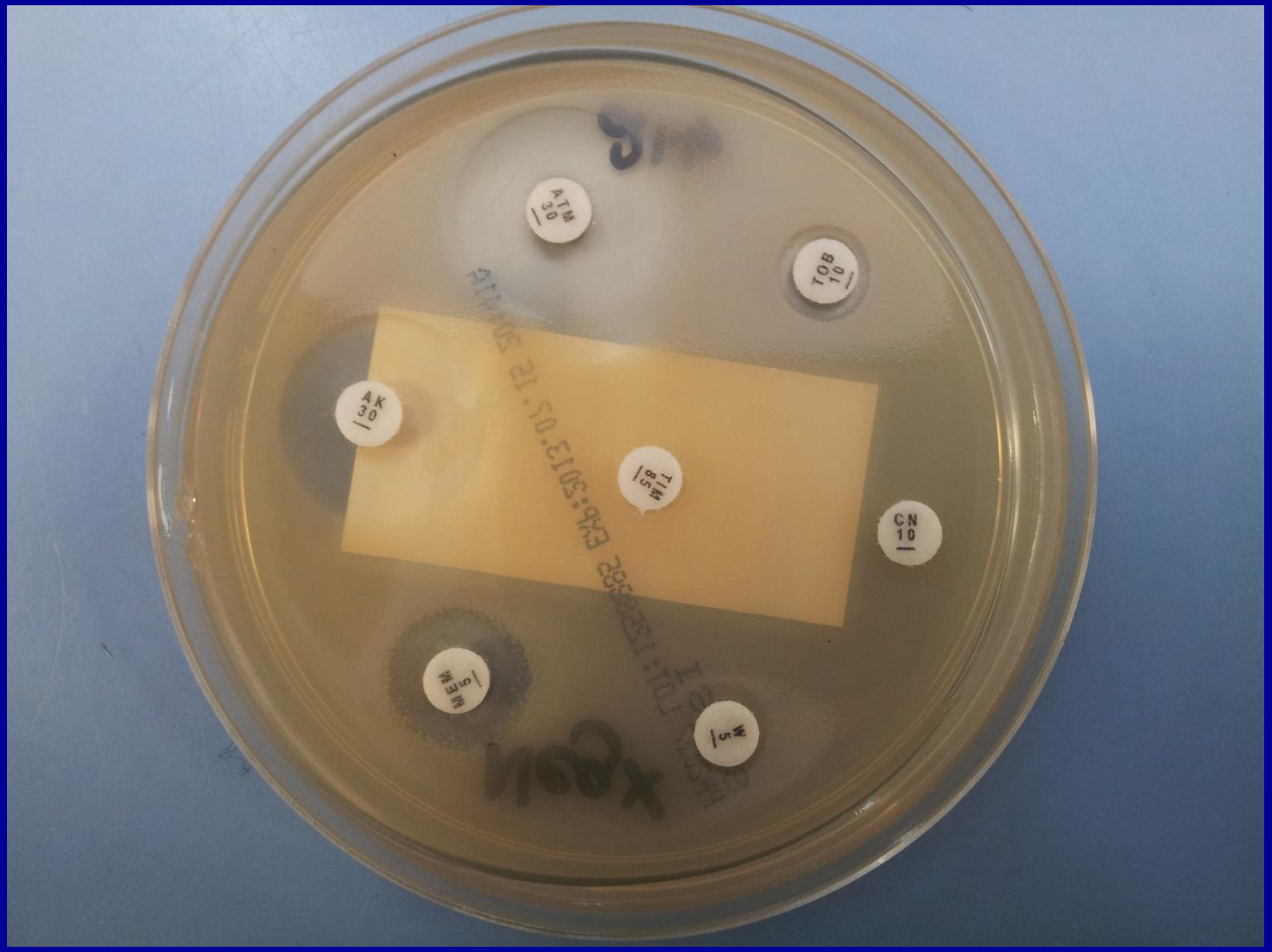
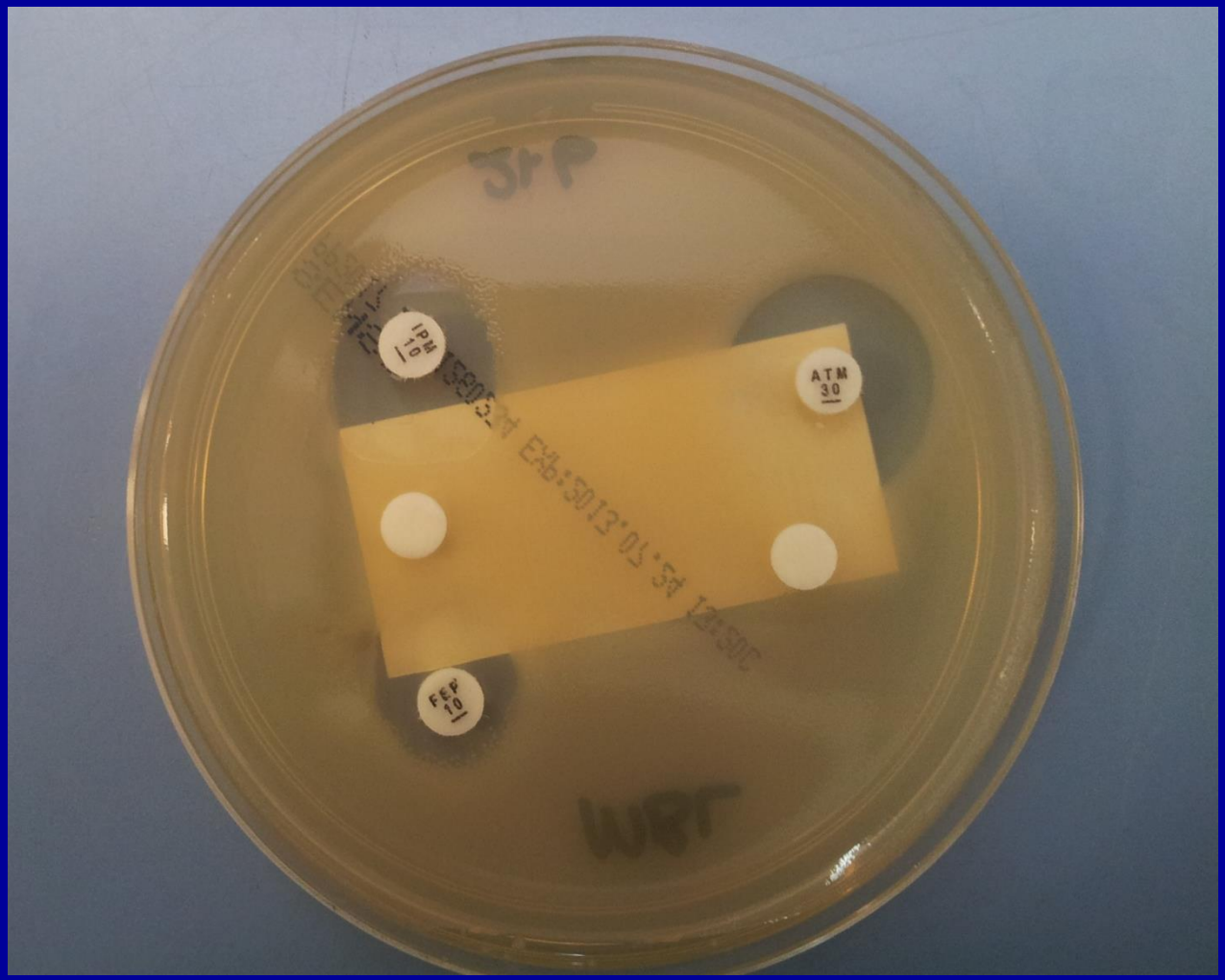


ESBL +ve

SEALS South *Enterobacter cloacae* isolate from catheter urine May 2013



PCR: IMP +ve

CRE Isolates SEALS South 2011-June 30 2013

Species	n
Enterobacter cloacae complex	11
Serratia marcescens	9
Citrobacter freundii	8
Klebsiella pneumoniae	7
Klebsiella oxytoca	7
Escherichia coli	5
Enterobacter aerogenes	2
Proteus mirabilis	1
Raoultella ornithinolytica	1

CRE Isolates SEALS South 2011-June 30 2013

Source of isolates	n
Urine	36
Wound swab	5
Sputum	3
Fluid/Pus	3
Blood culture	2
CAPD fluid	1
CVC tip	1

The Australian Group on Antimicrobial Resistance (AGAR)
Gram-negative Survey
2011 Antimicrobial Susceptibility Report

- 1,827 *E. coli*
- 537 *Klebsiella* spp.
- 269 *Enterobacter* spp.
- Vitek 2 and CLSI Jan 2012 breakpoints

- 8 $bla_{\text{IMP-4}}$ isolates
  - *K. pneumoniae* 4
  - *E. cloacae* 3
  - *K. oxytoca* 1

How well does CDS method detect CRE? RCPA QAP 2008: 6: 1B

- MBL +ve *Klebsiella pneumoniae* from urine
- 77/306 (25%) respondents used CDS
- CDS users
  - None reported Meropenem or Imipenem (S)
  - None reported (S) to β-lactams other than Aztreonam
- Other methods
  - 4/229 reported Meropenem (S)
  - 5/229 reported Imipenem (S)
  - 24/229 reported (S) to β-lactams other than Aztreonam

Source: Deb Walker, Senior Scientist, RCPA Microbiology QAP

How well does CDS detect CR-MRAB? RCPA QAP 2012: 7: 2B

- Multi-resistant (incl. Carbapenem-R) *Acinetobacter baumannii* from sputum
- 40/263 (15%) respondents used CDS

- CDS users
  - None reported Meropenem or Imipenem (S)
  - None reported (S) to other β-lactams
- Other methods
  - 1/223 reported Imipenem (S)
  - 1/223 reported (S) to Ceftazidime

Source: Deb Walker, Senior Scientist, RCPA Microbiology QAP

2nd reported NDM-1 producing isolate in Australia was detected in a lab using the CDS method

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Nov. 2010, p. 4914–4916 Vol. 54, No. 11
0066-4804/10/$12.00 doi:10.1128/AAC.00878-10
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Emergence of Metallo-β-Lactamase NDM-1-Producing Multidrug-Resistant *Escherichia coli* in Australia[▽]

Laurent Poirel,[1] Emilie Lagrutta,[1] Peter Taylor,[2] Jeanette Pham,[2] and Patrice Nordmann[1]*

Service de Bactériologie-Virologie, INSERM U914 "Emerging Resistance to Antibiotics," Hôpital de Bicêtre, Assistance Publique/Hôpitaux de Paris, Faculté de Médecine et Université Paris-Sud, K.-Bicêtre, France,[1] and Department of Microbiology, South Eastern Area Laboratory Services, Prince of Wales Hospital, Sydney, Australia[2]

Received 28 June 2010/Returned for modification 13 August 2010/Accepted 27 August 2010

A multidrug-resistant *Escherichia coli* isolate recovered in Australia produced a carbapenem-hydrolyzing β-lactamase. Molecular investigations revealed the first identification of the bla_{NDM-1} metallo-β-lactamase gene in that country. In addition, this *E. coli* isolate expressed the extended-spectrum β-lactamase CTX-M-15, together with two 16S rRNA methylases, namely, ArmA and RmtB, conferring a high level of resistance to aminoglycosides.

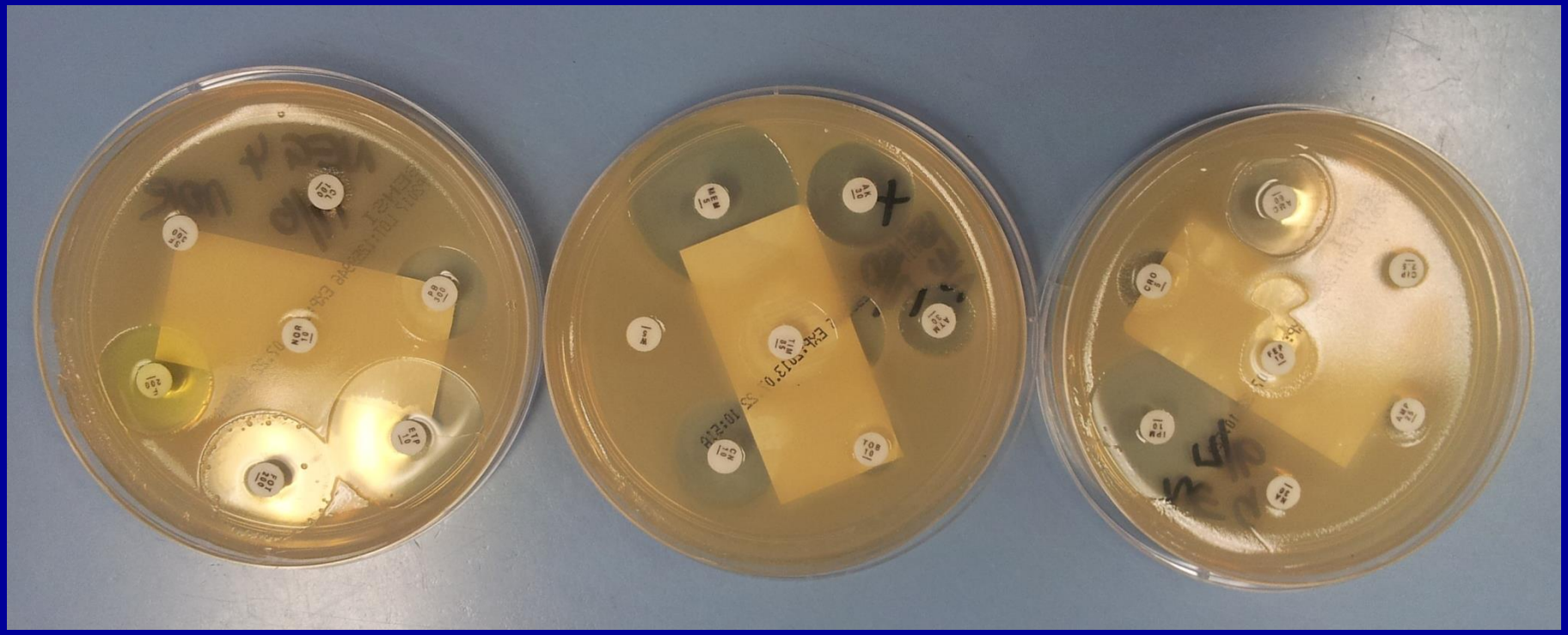
CDS method and ESBL detection

- SEALS South ESBL data
  - 3.7% of all Gram neg urine isolates 2012
  - 5% of all Gram neg blood culture isolates 2012

  - 5.9% of all Hospital-onset *E. coli* blood isolates 2012
  - 4.2% of all Community-onset *E. coli* blood isolates 2012

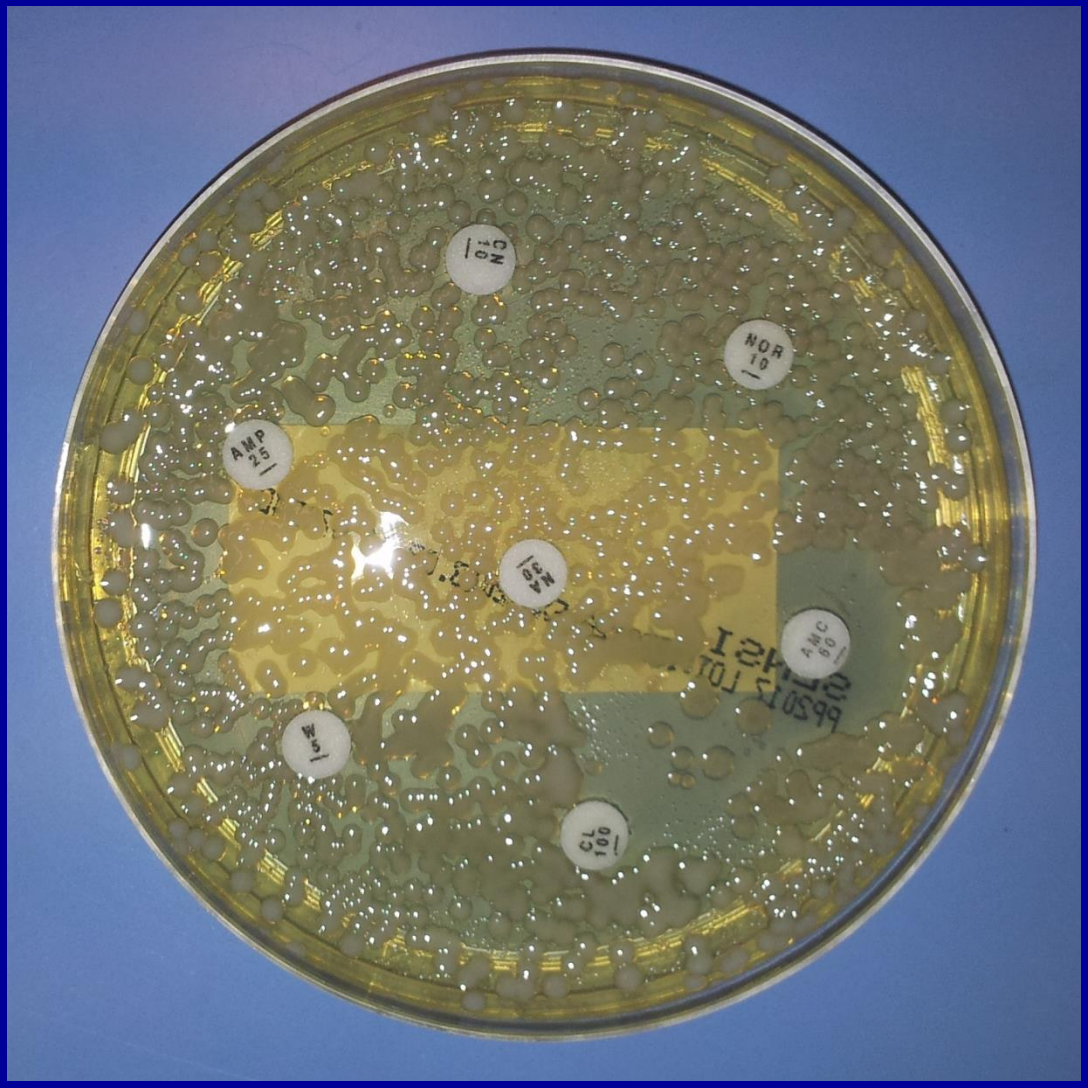
  - 12.9% of all *Enterobacter* spp., *Citrobacter freundii* & *Serratia marcescens* blood isolates 2007-2012

CDS method and ESBL detection

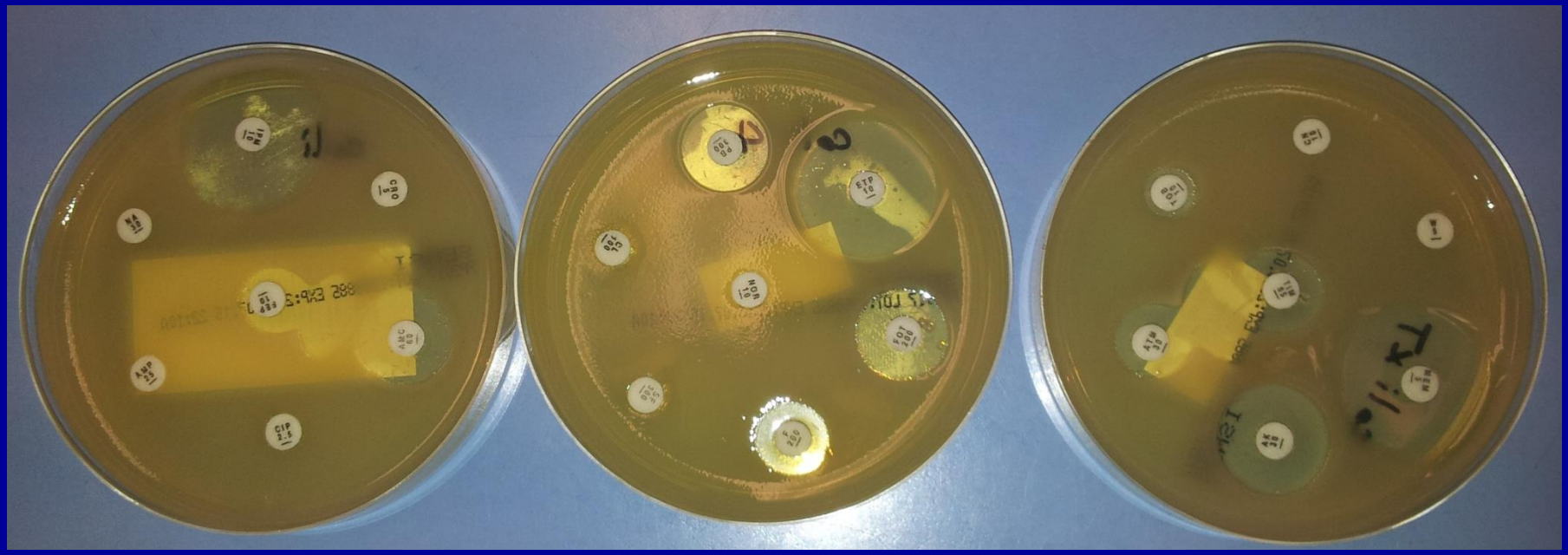


Confirmatory testing not necessary
with CDS recommended disc positioning

ESBL detection on direct urine susceptibility testing: CDS disc positioning important



Confirmed ESBL +ve *Klebsiella pneumoniae* in special care nursery



How well does CDS method detect ESBLs? RCPA QAP 2011: 6: 1B

- ESBL +ve *E. coli* from urine
- 50/299 (17%) respondents used CDS

- CDS users
  - 33/50 (66%) commented on ESBL production
  - None reported (S) to cephalosporins
- Other methods
  - 173/249 (69%) commented on ESBL production
  - 44/249 (18%) reported (S) to cephalosporins

Source: Deb Walker, Senior Scientist, RCPA Microbiology QAP

How well does CDS detect plasmid mediated AmpCs? RCPA QAP 2010: 6: 1B

- AmpC +ve, ESBL -ve *E. coli* from urine
- (R) to AMP, AMC, CL, CTX, CRO, CAZ
- (S) to FEP
- 60/306 (20%) respondents used CDS
- CDS users
  - None reported (S) to CL, CTX, CRO, CAZ
  - 7/60 (12%) reported ESBL +ve
- Other methods
  - 22/246 (9%) CTX/CRO (S); 19/246 (8%) CAZ (S)
  - 1/246 CL (S)
  - 40/246 (16%) reported ESBL +ve

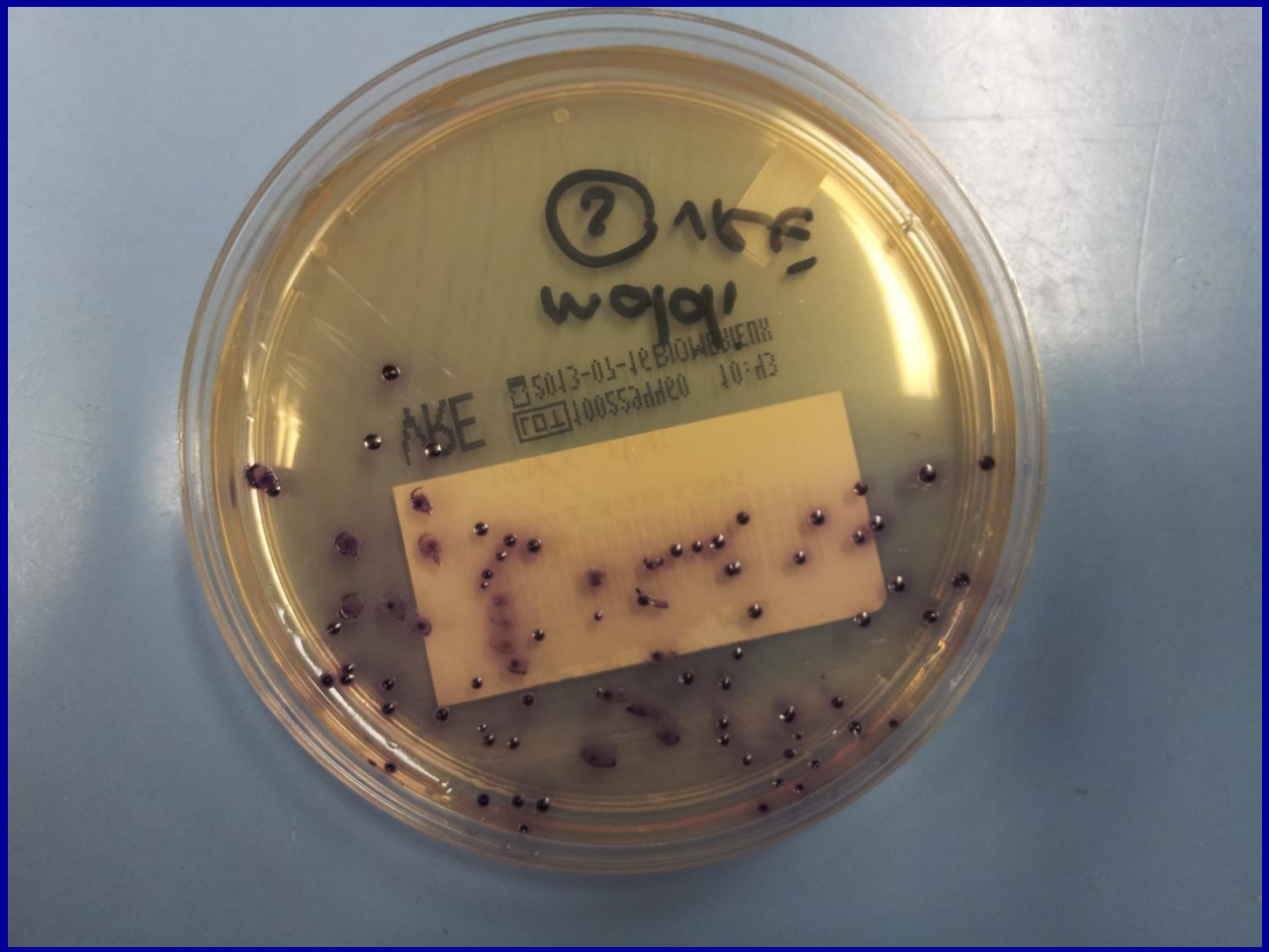
Source: Deb Walker, Senior Scientist, RCPA Microbiology QAP

How well does CDS detect VRE? RCPA QAP 2010: 1: 4

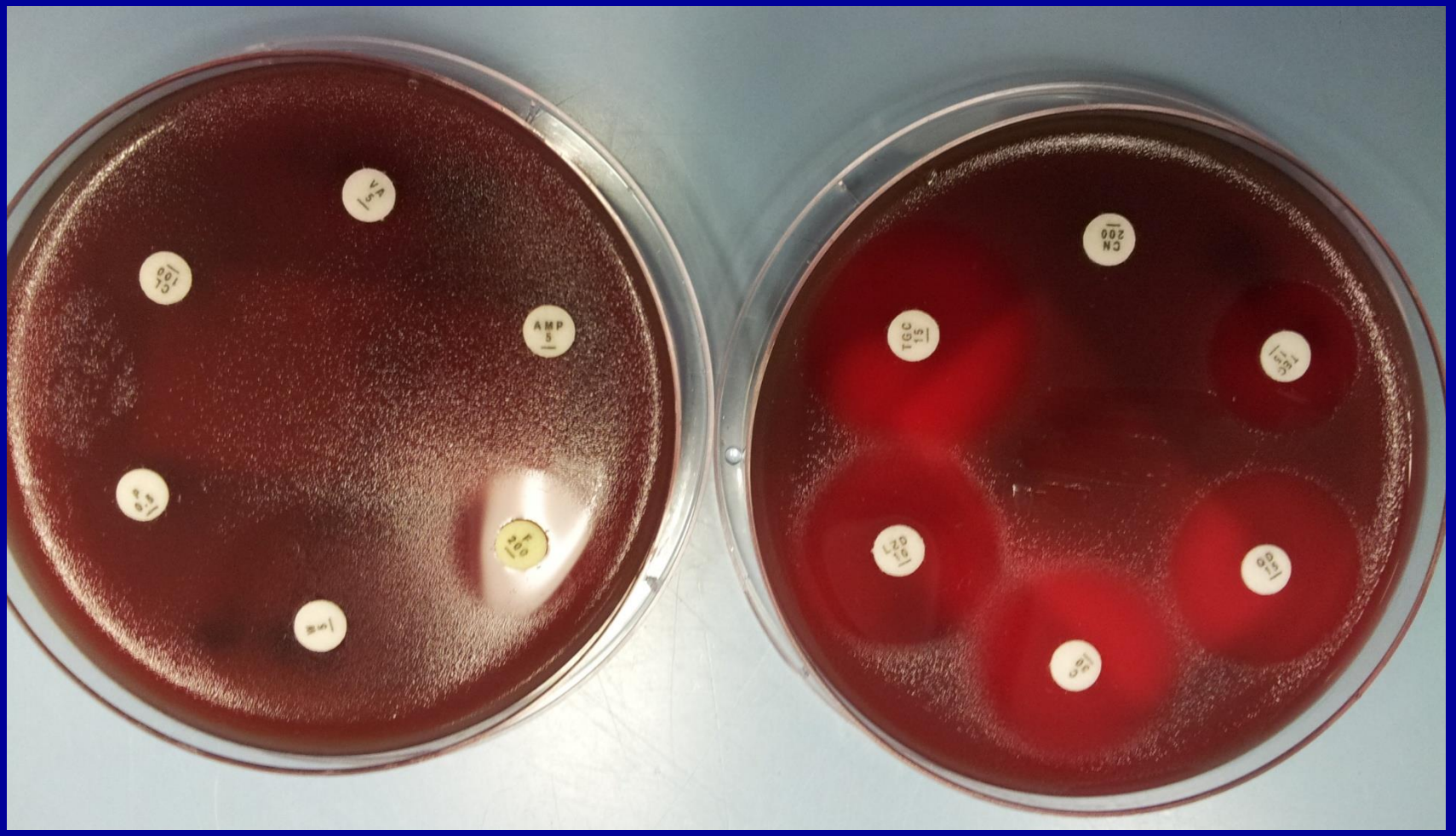
- Vancomycin resistant *Enterococcus faecium* from a wound swab
- Van B phenotype
  - Vancomycin M.I.C.=16 mg/L
  - Teicoplanin M.I.C.=1.0 mg/L
- CDS users
  - 55/60 (92%) reported VRE
- Other methods
  - 135/196 (73%) reported VRE

Source: Deb Walker, Senior Scientist, RCPA Microbiology QAP

VRE detection SEALS South

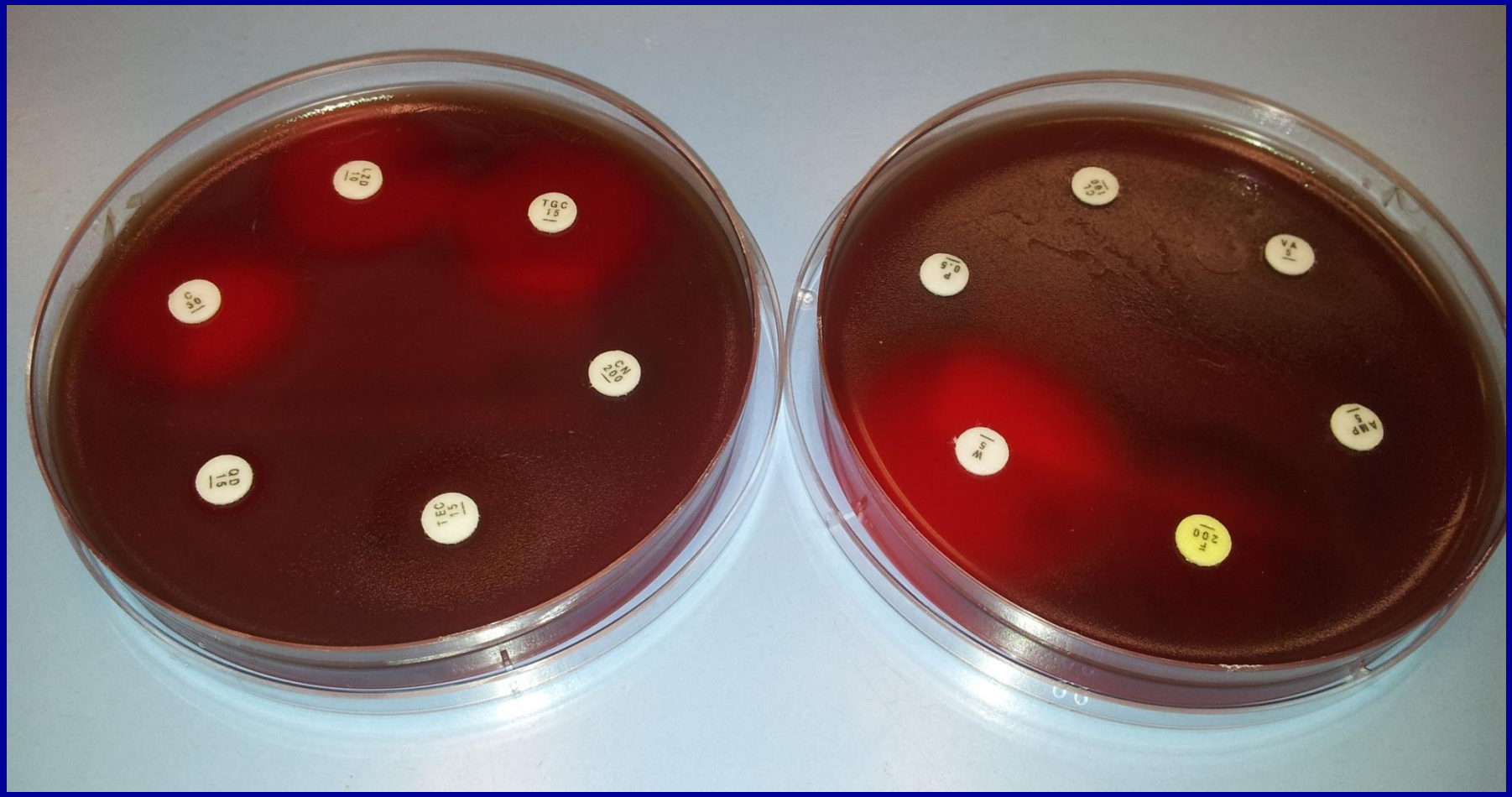


VRE detection SEALS South



Van B VR *E. faecium*

VRE detection SEALS South



Van A VR *E. faecium*

How well does CDS detect inducible clindamycin resistance? RCPA QAP 2012: 8: 3

- *Streptococcus pyogenes* from a skin swab
- Erythromycin resistant with inducible clindamycin resistance
- $iMLS_B$ (inducible Macrolide, Lincosamide, Streptogramin B) phenotype
- CDS users
  - 3/49 (6%) reported Erythromycin (S)
  - 2/49 (4%) reported Clindamycin (S)
- Other methods
  - 28/172 (16%) reported Erythromycin (S)
  - 38/172 (22%) reported Clindamycin (S)

Source: Deb Walker, Senior Scientist, RCPA Microbiology QAP

EUCAST may not have all the answers

MOVING TO EUCAST - A STATEWIDE SERVICE APPROACH CONT'D

Narelle GEORGE, Supervising Scientist, Microbiology, Pathology Queensland, HSSA, Brisbane, Queensland, 4029

Table 1: Non-EUCAST Calibrated Organisms tested by Pathology Queensland

ORGANISM	ACTION
Aeromonas species Plesiomonas Vibrio species	Use CLSI M45-A2
Burkholderia cepacia	*Use CLSI M100-S23*
Burkholderia pseudomallei	Use CLSI M45-A2
Non-fermenting GNB (Achromobacter, Alcaligenes, Chryseobacterium, etc)	*Use EUCAST Non species Specific Breakpoints + Comment Non standardised testing performed*
HACEK Group *Pasteurella sp******	Use CLSI M45-A2 (*EUCAST V3.1* now has calibration criteria)
Corynebacterium sp	*Use CLSI M45-A2*
Bacillus species (B anthracis)	Use CLSI M100-S23
Streptococcus milleri	*Use CLSI M100-S23*
Abiotrophia, Granulicatella	Use CLSI M45-A2
Leuconostoc sp Pediococcus sp	Use CLSI M45-A2
Lactobacillus sp	Use CLSI M45-A2
Erysipelothrix rhusiopathiae	Use CLSI M45-A2

CDS Method

Source: George, N. Breakpoint (ASA Newsletter) 2013-Issue 02

EUCAST may not have all the answers

Table 2: Antibiotics Tested by Pathology Queensland not Calibrated by EUCAST

ORGANISM	ANTIBIOTIC	ACTION
Staphylococcus aureus	Nitrofurantoin (urines)	EUCAST only available for *Staph saprophyticus*
Enterococcus species	Daptomycin	Use CLSI
Enterobacteriaceae	Cefazolin	Urines – test cefalexin by disc instead (EUCAST calibrated)
	Cefoxitin screen only	Use <8 breakpoint - same as CLSI
	ESBL screen	Still test report if positive, If negative Add comment
Pseudomonas aeruginosa	Norfloxacin	Use CLSI
Stenotrophomonas maltophilia	Ticarcillin-clavulanate	Use CLSI
	Ceftazidime	Use CLSI
Acinetobacter species	Ampicillin, Amoxicillin-clavulanate, Ticarcillin-clavulanate, Piperacillin-tazobactam, third generation cephalosporins, cefepime	Use CLSI where published breakpoints are available

CDS Method

Source: George, N. Moving to EUCAST – a statewide service approach. Breakpoint (ASA Newsletter) 2013-Issue 02

Conclusion

- With all it's unique advantages including an Australian reference lab availability
- With its good performance in the QAP in our lab and others
- With its ability to economically detect resistance & resistance mechanisms of clinical & infection control importance

… why not use the CDS method.