

Anaerobe Working Group

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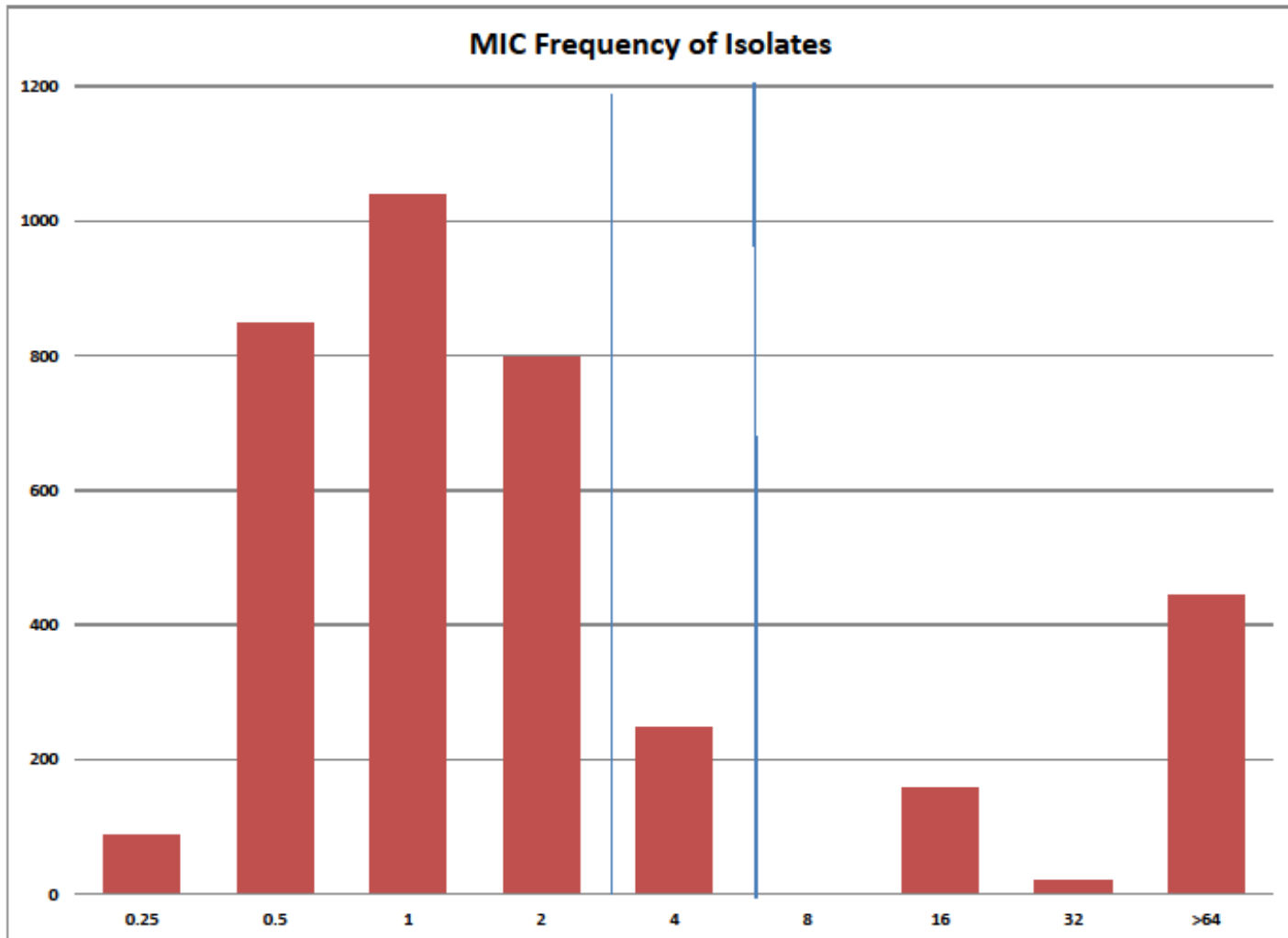
Meredith Hackel

ECOFF – Vancomycin – Anaerobic Gram-Positive Bacteria

a. Published Data Summary

- i. Evaluated 12 Studies (reference list provided)
- ii. Data from Europe, United States and Kuwait
- iii. Data from 2004 to 2014
- iv. 4037 isolates
- v. 46 grouping (genus or species)

Summary of Data to Support ECOFF



What species at MIC 90 at 4 µg/ml

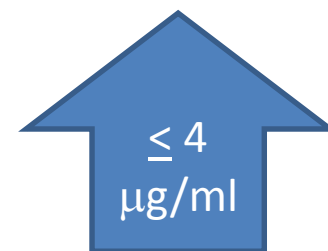
- *Lactobacillus* species
- *Eubacterium limosum*
- *Eggerthella lenta*
- *Clostridium ramosum*
- *Clostridium paraputrificum*
- *Clostridium difficile*

Clostridium difficile

Ref	N	0.125	0.25	0.5	1	2	4	8	16
2	556				50	90			
12	15				50/90				
5	72				50	90			
6	14			50	90				
11	102			50	90				
4	28		50	90					
7	50				50		90		
3	50				50	90			

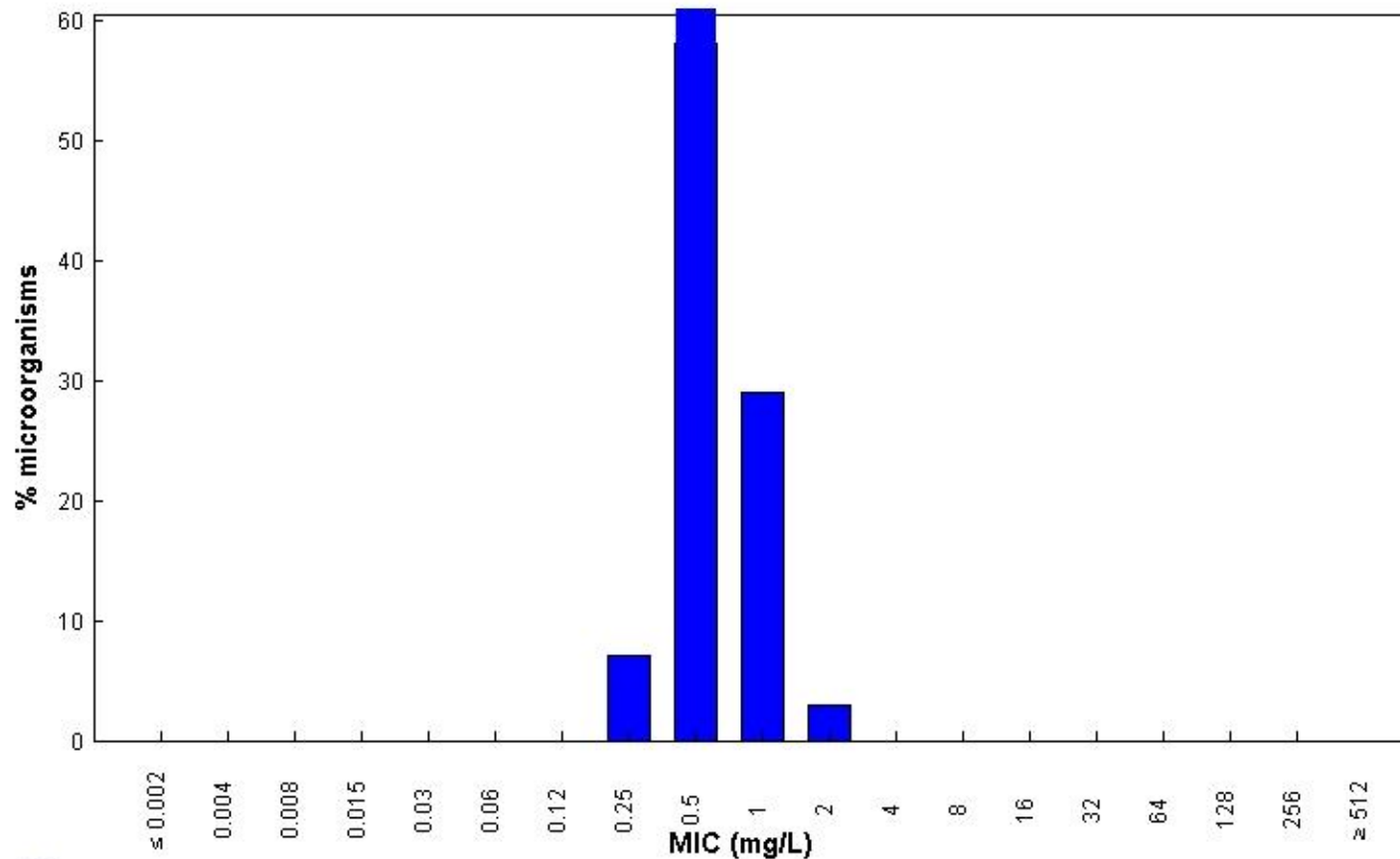
Total N=887

EUCAST ECOFF $\leq 2\mu\text{g/ml}$



Vancomycin / *Clostridium difficile*
International MIC Distribution - Reference Database 2014-06-30

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance



X	Y
0.002	0
0.004	0
0.008	0
0.016	0
0.032	4
0.064	2
0.125	12
0.25	353
0.5	2889
1	1451
2	197
4	16
8	3
16	1
32	0
64	0
128	0
256	0
512	0

MIC

Epidemiological cut-off (ECOFF): 2 mg/L

Wildtype (WT) organisms: ≤ 2 mg/L

4928 observations (9 data sources)

Vote requested

a. Vancomycin ECOFF

a. C. difficile ≤ 4 S

b. Add to M100 Table 2J

c. Footnote added to breakpoint in the table.

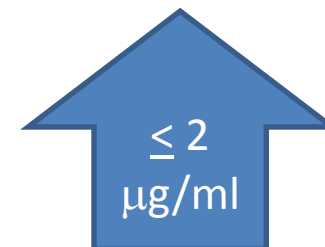
“The breakpoints are based on the epidemiologic cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.”

Propionibacterium acnes

Ref	N	0.06	0.125	0.25	0.5	1	2	4	8	16
10	304			50	90					
11	101		50	90						
4	11		50	90						
6	12			50	90					

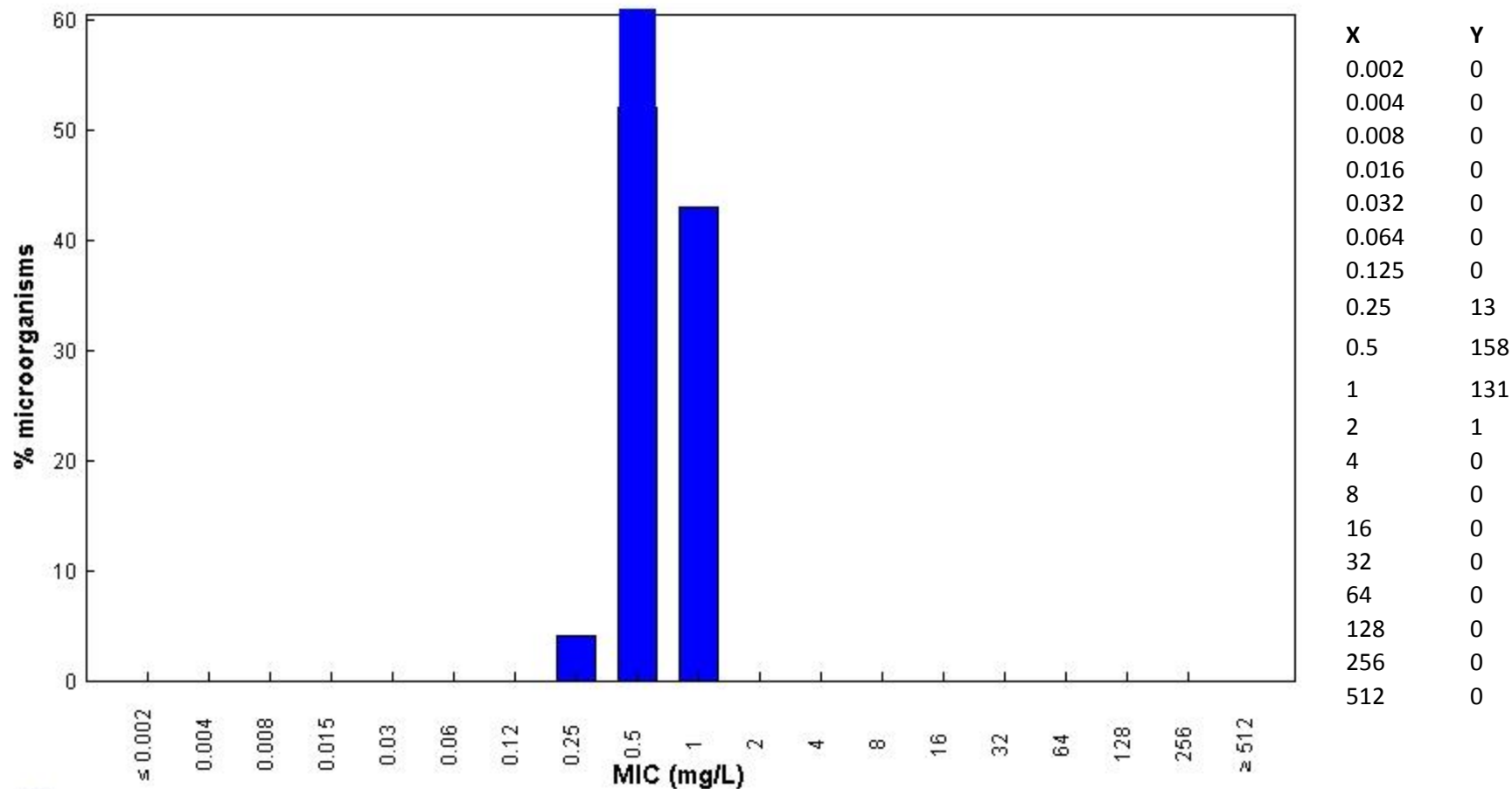
Total N=428

Breakpoints same as EUCAST breakpoints



Vancomycin / *Propionibacterium acnes*
International MIC Distribution - Reference Database 2014-06-30

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance



MIC
 Epidemiological cut-off (ECOFF): 2 mg/L
 Wildtype (WT) organisms: ≤ 2 mg/L

303 observations

Vote requested

a. Vancomycin ECOFF

a. P. acnes ≤ 2 S

b. Add to M100 Table 2J

c. Footnote added to breakpoint in the table. “The breakpoints are based on the epidemiologic cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.”

Revisions for Appendix D – 2010, 2011 and 2012 data

Appendix D. Cumulative Antimicrobial Susceptibility Report for Anaerobic Organisms

Isolates collected from selected US hospitals
1 January 2010 – 31 December 2012^a

Bacteroides fragilis Group

Anaerobic Organisms	Number of Strains	Ampicillin- sulbactam		Number of Strains	Piperacillin- tazobactam		Number of Strains	Cefoxitin		Number of Strains	Ertapenem		Number of Strains	Imipenem		Number of Strains	Meropenem	
		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R
Percent Susceptible (%S) and Percent Resistant (%R) ^c																		
Breakpoints in µg/mL		≤8/4	≥32/16		≤32/4	≥128/4		≤16	≥64		≤4	≥16		≤4	≥16		≤4	≥16
<i>B. fragilis</i>	768	90	3	1497	98	1	1403	87	3	770	97	2	234	98	1	1503	96	1
<i>B. thetaiotaomicron</i>	349	80	4	467	79	8	469	48	8	348	98	1	134	99	1	470	98	1
<i>B. ovatus</i>	77	88	1	127	95	4	130	58	9	77	95	1	52	100	0	130	98	0
<i>B. vulgatus</i>	106	70	5	174	97	2	153	82	7	106	99	1	56	100	0	153	98	1
<i>B. uniformis</i>	94	88	4	128	95	2	129	60	9	94	100	0	24	100	0	128	99	0
<i>B. eggerthii</i>	60	93	0	70	89	11	73	34	21	60	100	0	—	—	—	72	100	0
<i>Parabacteroides distasonis</i>	220	66	20	265	56	30	265	42	15	220	97	2	33	97	0	265	97	2
<i>B. fragilis</i> group without <i>B. fragilis</i>	906	78	8	1231	81	11	1219	53	10	905	98	1	299	99	0	1218	98	1
<i>B. fragilis</i> group (all 7 species listed)	2580	82	6	3959	87	7	3841	65	7	2580	98	1	832	99	1	3939	98	1

Revisions for Appendix D – 2010, 2011 and 2012 data

Appendix D. (Continued)

Bacteroides fragilis Group (Continued)

Anaerobic Organisms	Number of Strains	Clindamycin		Number of Strains	Moxifloxacin		Number of Strains	Metronidazole ^b	
Percent Susceptible (%S) and Percent Resistant (%R) ^c		%S	%R		%S	%R		%S	%R
Breakpoints in µg/mL		≤2	≥8		≤2	≥8		≤8	≥32
<i>B. fragilis</i>	1423	72	23	769	65	26	1503	96	2
<i>B. thetaiotaomicron</i>	469	32	55	348	47	34	470	100	0
<i>B. ovatus</i>	129	43	46	77	32	40	130	99	0
<i>B. vulgatus</i>	152	47	52	92	20	76	174	100	0
<i>B. uniformis</i>	121	44	40	94	27	53	128	99	0
<i>B. eggerthii</i>	72	29	63	61	25	38	72	100	0
<i>Parabacteroides distasonis</i>	265	25	57	220	69	27	265	100	0
<i>B. fragilis</i> group without <i>B. fragilis</i>	1208	35	53	892	45	40	1239	100	0 ^{a.}
<i>B. fragilis</i> group (all 7 species listed)	3839	48	42	2553	51	36	3981	98	1 ^{a.}

a. Data were generated from unique isolates from patient specimens submitted to **four** laboratories: Tufts New England Medical Center, Boston, MA; Loyola University Medical Center, Maywood, IL; **International Health Management Associates Inc., Schaumburg, IL** and R.M. Alden Research Laboratory, Culver City, CA. Testing was performed by the agar dilution method.

b. Resistance to metronidazole occurs infrequently.

c. Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.

Revisions for Appendix D – 2010, 2011 and 2012 data

Appendix D. (Continued)

Isolates collected from selected US hospitals
1 January 2010 – 31 December 2012^a

Anaerobic Organisms Other Than *Bacteroides fragilis* Group

Anaerobic Organisms	Number of Strains	Ampicillin-sulbactam		Number of Strains	Piperacillin-tazobactam		Number of Strains	Cefoxitin		Number of Strains	Ertapenem		Number of Strains	Meropenem	
Percent Susceptible (%S) and Percent Resistant (%R) ^d		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R
Breakpoints in µg/mL		≤8/4	≥32/16		≤32/4	≥128/4		≤16	≥64		≤4	≥16		≤4	≥16
<i>Prevotella</i> spp.	229	99	0	800	100	0	806	97	1	196	100	0	234	100	0
<i>Fusobacterium nucleatum-necrophorum</i>	27	100	0	27	100	0	27	100	0	15	100	0	27	100	0
Anaerobic gram-positive cocci ^e	150	88	9	614	99	0	148	94	3	150	83	9	614	98	1
<i>Veillonella</i> spp. ^b	31	90	6	32	84	16	32	97	0	26	85	8	32	97	0
<i>P. acnes</i>	58	100	0	58	100	0	58	100	0	58	100	0	58	100	0
<i>Clostridium perfringens</i>	108	100	0	348	100	0	108	99	0	69	100	0	348	100	0
<i>C. difficile</i> ^c	34	100	0	494	99	1	34	3	97	24	100	0	494	93	0
Other <i>Clostridium</i> spp.	71	100	0	266	98	2	77	70	17	39	100	0	266	99	0

Revisions for Appendix D – 2010, 2011 and 2012 data

Appendix D. (Continued)
Anaerobic Organisms Other Than *Bacteroides fragilis* Group

Anaerobic Organisms	Number of Strains	Clindamycin		Number of Strains	Moxifloxacin		Number of Strains	Metronidazole	
Percent Susceptible (%S) and Percent Resistant (%R) ^d		%S	%R		%S	%R		%S	%R
Breakpoints in µg/mL		≤2	≥8		≤2	≥8		≤8	≥32
<i>Prevotella</i> spp.	800	72	26	196	73	24	571	97	0
<i>Fusobacterium nucleatum- necrophorum</i>	27	100	0	15	100	0	27	100	0
Anaerobic gram- positive cocci ^e	614	79	16	150	63	20	611	96	3
<i>Veillonella</i> spp. ^b	32	66	34	26	81	12	32	97	0
<i>P. acnes</i>	58	91	9	58	93	3	58	9	91
<i>Clostridium perfringens</i>	348	86	7	69	100	0	348	100	0
<i>C. difficile</i> ^c	493	38	48	17	94	6	494	100	0
Other <i>Clostridium</i> spp.	266	66	21	45	74	20	266	98	1

- Data were generated from unique isolates from patient specimens submitted to **four** laboratories: Tufts New England Medical Center, Boston, MA; Loyola University Medical Center, Maywood, IL; **International Health Management Associates Inc., Schaumburg, IL** and R.M. Alden Research Laboratory, Culver City, CA. Testing was performed by the agar dilution method.
- Calculated from fewer than the CLSI document M39¹ recommendation of 30 isolates.
- C. difficile* isolates are from intestinal source; these results do not imply efficacy for intraluminal infections. Vancomycin minimal inhibitory concentrations for all isolates were <4 µg/mL.
- Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.
- Anaerobic gram-positive cocci include *Peptococcus*, *Peptostreptococcus*, *Fingoldia*, *Peptoniphilus*, and *Anaerococcus* species.

Reference

- CLSI. *Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition*. CLSI document M39-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

Broth Microdilution – other than *B. fragilis*

- Currently evaluating
 - Data previously collected by the working group
 - New data from drug study
- Looking at grouping at higher level than species
- No financial support to conduct new studies
- No progress made on this item, will continue to work on between now and January Meeting.
Next working group meeting has been schedule for July 21st.

Future projects

- Intrinsic resistance for anaerobes
- ECOFFs for other gram-positive species and vancomycin

Clostridium species

[illegible]

C. clostridioforme data

Clostridium clostridioforme	1	1	0.5-1	20
Clostridium clostridioforme	0.5	1	0.25-1	21
Clostridium clostridioforme	16	>2048	8->2048	7
Clostridium clostridioforme	0.5	1	0.25->32	15

Revised wording for Comments and Notes

- 4 requests were submitted for clarification
- Revisions were created by the Anaerobe Adhoc Working Group
- Approved in content by Methods Working Group
- Deferred to Text and Tables for final wording